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(54) **3-(3H-IMIDAZO[4,5-C]PYRIDIN-2-YL)-1H-PYRAZOLO[3,4-C]PYRIDINE AND THERAPEUTIC USES THEREOF**

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(57) **ABSTRACT**

Azaindazole compounds for treating various diseases and pathologies are disclosed. More particularly, the present invention concerns the use of an azaindazole compound or analogs thereof, in the treatment of disorders characterized by the activation of Wnt pathway signaling (e.g., cancer, abnormal cellular proliferation, angiogenesis, fibrotic disorders, bone or cartilage diseases, and osteoarthritis), the modulation of cellular events mediated by Wnt pathway signaling, as well as genetic diseases and neurological conditions/disorders/diseases due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Also provided are methods for treating Wnt-related disease states.

31 Claims, No Drawings

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3-(3H-IMIDAZO[4,5-C]PYRIDIN-2-YL)-1H-PYRAZOLO[3,4-C]PYRIDINE AND THERAPEUTIC USES THEREOF

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 62/047,438, filed Sep. 8, 2014, which is incorporated herein by reference in its entirety.

BACKGROUND

1. Technical Field

This disclosure relates to inhibitors of one or more proteins in the Wnt pathway, including inhibitors of one or more Wnt proteins, and compositions comprising the same. More particularly, it concerns the use of an azaindazole compound or salts or analogs thereof, in the treatment of disorders characterized by the activation of Wnt pathway signaling (e.g., cancer, abnormal cellular proliferation, angiogenesis, fibrotic disorders, bone or cartilage diseases, and osteoarthritis), the modulation of cellular events mediated by Wnt pathway signaling, as well as genetic diseases and neurological conditions/disorders/diseases due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Also provided are methods for treating Wnt-related disease states.

2. Background

The Wnt growth factor family includes more than 10 genes identified in the mouse and at least 19 genes identified in the human. Members of the Wnt family of signaling molecules mediate many short- and long-range patterning processes during invertebrate and vertebrate development. The Wnt signaling pathway is known for its role in the inductive interactions that regulate growth and differentiation, and it also plays roles in the homeostatic maintenance of post-embryonic tissue integrity. Wnt stabilizes cytoplasmic β-catenin, which stimulates the expression of genes including c-myc, c jun, fra-1, and cyclin Dl. In addition, misregulation of Wnt signaling can cause developmental defects and is implicated in the genesis of several human cancers. The Wnt pathway has also been implicated in the maintenance of stem or progenitor cells in a growing list of adult tissues including skin, blood, gut, prostate, muscle, and the nervous system.

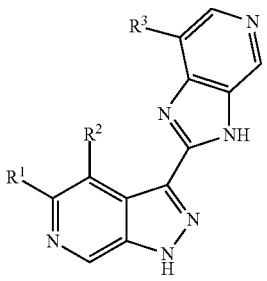
SUMMARY

The present disclosure provides methods and reagents, involving contacting a cell with an agent, such as an azaindazole compound, in a sufficient amount to antagonize a Wnt activity, e.g., to reverse or control an aberrant growth state or correct a genetic disorder due to mutations in Wnt signaling components.

Some embodiments disclosed herein include Wnt inhibitors containing an azaindazole core. Other embodiments disclosed herein include pharmaceutical compositions and methods of treatment using these compounds.

One embodiment disclosed herein includes a compound having the structure of Formula I:

I



as well as prodrugs and pharmaceutically acceptable salts thereof.

In some embodiments of Formula (I):

R^1 is selected from the group consisting of -heteroaryl $(R^4)_q$ and -heterocyclyl$(R^5)_h$;

R^2 is selected from the group consisting of H and halide;

R^3 is selected from the group consisting of -heteroaryl $(R^6)_q$, -heterocyclyl$(R^7)_h$, and -aryl$(R^8)_k$;

each R^4 is one substituent attached to the heteroaryl and is independently selected from the group consisting of halide, —$(C_{1-6}$alkyl), —$(C_{1-4}$alkylene$)_p$heterocyclyl$(R^9)_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{10})_j$, —$(C_{1-4}$ alkylene$)_p$aryl $(R^{11})_k$, —NHC(=O)R^{12}, —$NR^{13}R^{14}$, —$(C_{1-6}$ alkylene) $NR^{15}R^{16}$, and —OR^{22};

each R^5 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —OCH_3, —CN, and —C(=O)R^{17};

each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, and —OCH_3;

each R^8 is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, —OCH_3, —$(C_{1-6}$alkylene$)_p$ $NHSO_2R^{17}$, —$NR^{13}(C_{1-6}$ alkylene)$NR^{13}R^{14}$, —$(C_{1-6}$ alkylene$)_pNR^{13}R^{14}$, and —OR^{25};

each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{10} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{11} is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{12} is independently selected from the group consisting of —$(C_{1-9}$alkyl), -heteroaryl$(R^{18})_q$, -aryl$(R^{19})_k$, —CH_2aryl$(R^{19})_k$, -carbocyclyl$(R^{20})_j$, —CH_2carbocyclyl $(R^{20})_j$, —$(C_{1-4}$ alkylene$)_pNR^{23}R^{24}$, -heterocyclyl$(R^{21})_h$, and —CH_2heterocyclyl$(R^{21})_h$;

each R^{13} is independently selected from the group consisting of H and —$(C_{1-6}$alkyl);

each R^{14} is independently selected from the group consisting of H, —$(C_{1-6}$alkyl), —CH_2aryl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$;

each R^{15} is independently selected from the group consisting of H and —$(C_{1-6}$alkyl);

each R^{16} is independently selected from the group consisting of H, —$(C_{1-6}$alkyl), —CH_2aryl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$;

each R^{17} is a —(C_{1-6}alkyl);

each R^{18} is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{19} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{20} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{21} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{22} is independently selected from the group consisting of H, —(C_{1-6}alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{21})$_h$, —(C_{1-4}alkylene)$_p$carbocyclyl(R^{20})$_j$, —(C_{1-4} alkylene)$_p$aryl(R^{19})$_k$, and —(C_{1-6}alkylene)$_p$$NR^{23}R^{24}$;

each R^{23} is independently selected from the group consisting of H and —(C_{1-6}alkyl);

each R^{24} is independently selected from the group consisting of H and —(C_{1-6}alkyl);

each R^{25} is independently selected from the group consisting of H, —(C_{1-6}alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{21})$_h$, and —(C_{1-6} alkylene)$_p$$NR^{23}R^{24}$;

each p is independently 0 or 1;

each q is independently 0 to 4;

each h is independently 0 to 10;

each k is independently 0 to 5; and

each j is independently 0 to 12.

Some embodiments include stereoisomers and pharmaceutically acceptable salts of a compound of Formula (I).

Some embodiments include pro-drugs of a compound of Formula (I).

Some embodiments of the present disclosure include pharmaceutical compositions comprising a compound of Formula (I) and a pharmaceutically acceptable carrier, diluent, or excipient.

Other embodiments disclosed herein include methods of inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins by administering to a patient affected by a disorder or disease in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, cell cycling and mutations in Wnt signaling components, a compound according to Formula (I). Accordingly, the compounds and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation and correct a genetic disorder due to mutations in Wnt signaling components.

Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, osteochondrodysplasia, Alzheimer's disease, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-Amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

Some embodiments of the present disclosure include methods to prepare compounds of Formula (I).

It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

DETAILED DESCRIPTION

Provided herein are compositions and methods for inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins. Other Wnt inhibitors and methods for using the same are disclosed in U.S. application Ser. Nos. 12/852,706; 12/968,505; 13/552,188; 13/800,963; 13/855,874; 13/887,177 13/938,691; 13/938,692; 14/019,103; 14/019,147; 14/019,940; 14/149,948; 14/178,749; 14/331,427; and 14/334,005; and U.S. Provisional Application Ser. Nos. 61/232,603; 61/288,544; 61/305,459; 61/620,107; 61/642,915; and 61/750,221, all of which are incorporated by reference in their entirety herein.

Some embodiments provided herein relate to a method for treating a disease or disorder including, but not limited to, cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, osteoarthritis, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

In some embodiments, non-limiting examples of bone and cartilage diseases which can be treated with the compounds and compositions provided herein include bone spur (osteophytes), craniosynostosis, fibrodysplasia ossificans progressive, fibrous dysplasia, giant cell tumor of bone, hip labral tear, meniscal tears, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), osteochondritis dissecans, osteochondroma (bone tumor), osteopetrosis, relapsing polychondritis, and Salter-Harris fractures.

In some embodiments, pharmaceutical compositions are provided that are effective for treatment of a disease of an animal, e.g., a mammal, caused by the pathological activation or mutations of the Wnt pathway. The composition includes a pharmaceutically acceptable carrier and a compound as described herein.

DEFINITIONS

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly

understood by one of ordinary skill in the art to which this disclosure belongs. All patents, applications, published applications, and other publications are incorporated by reference in their entirety. In the event that there is a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

As used herein, "alkyl" means a branched, or straight chain chemical group containing only carbon and hydrogen, such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl and neo-pentyl. Alkyl groups can either be unsubstituted or substituted with one or more substituents. Alkyl groups can be saturated or unsaturated (e.g., containing —C═C— or —C≡C— subunits), at one or several positions. In some embodiments, alkyl groups include 1 to 9 carbon atoms (for example, 1 to 6 carbon atoms, 1 to 4 carbon atoms, or 1 to 2 carbon atoms).

As used herein, "alkylene" means a bivalent branched, or straight chain chemical group containing only carbon and hydrogen, such as methylene, ethylene, n-propylene, iso-propylene, n-butylene, iso-butylene, sec-butylene, tert-butylene, n-pentylene, iso-pentylene, sec-pentylene and neo-pentylene. Alkylene groups can either be unsubstituted or substituted with one or more substituents. Alkylene groups can be saturated or unsaturated (e.g., containing —C═C— or —C≡C— subunits), at one or several positions. In some embodiments, alkylene groups include 1 to 9 carbon atoms (for example, 1 to 6 carbon atoms, 1 to 4 carbon atoms, or 1 to 2 carbon atoms).

As used herein, "carbocyclyl" means a cyclic ring system containing only carbon atoms in the ring system backbone, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cyclohexenyl. Carbocyclyls may include multiple fused rings. Carbocyclyls may have any degree of saturation provided that at least one ring in the ring system is not aromatic. Carbocyclyl groups can either be unsubstituted or substituted with one or more substituents. In some embodiments, carbocyclyl groups include 3 to 10 carbon atoms, for example, 3 to 6 carbon atoms.

As used herein, "lower alkyl" means a subset of alkyl having 1 to 3 carbon atoms, which is linear or branched. Examples of lower alkyls include methyl, ethyl, n-propyl and isopropyl. Likewise, radicals using the terminology "lower" refer to radicals having 1 to about 3 carbons in the alkyl portion of the radical.

As used herein, "aryl" means a mono-, bi-, tri- or polycyclic group with only carbon atoms present in the ring backbone having 5 to 14 ring atoms, alternatively 5, 6, 9, or 10 ring atoms; and having 6, 10, or 14 pi electrons shared in a cyclic array; wherein at least one ring in the system is aromatic. Aryl groups can either be unsubstituted or substituted with one or more substituents. Examples of aryl include phenyl, naphthyl, tetrahydronaphthyl, 2,3-dihydro-1H-indenyl, and others. In some embodiments, the aryl is phenyl.

As used herein, "arylalkyl" means an aryl-alkyl-group in which the aryl and alkyl moieties are as previously described. In some embodiments, arylalkyl groups contain a C_{1-4}alkyl moiety. Exemplary arylalkyl groups include benzyl and 2-phenethyl.

As used herein, the term "heteroaryl" means a mono-, bi-, tri- or polycyclic group having 5 to 14 ring atoms, alternatively 5, 6, 9, or 10 ring atoms; and having 6, 10, or 14 pi electrons shared in a cyclic array; wherein at least one ring in the system is aromatic, and at least one ring in the system contains one or more heteroatoms independently selected from the group consisting of N, O, and S. Heteroaryl groups can either be unsubstituted or substituted with one or more substituents. Examples of heteroaryl include thienyl, pyridinyl, furyl, oxazolyl, oxadiazolyl, pyrrolyl, imidazolyl, triazolyl, thiodiazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyranyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, thiazolyl benzothienyl, benzoxadiazolyl, benzofuranyl, benzimidazolyl, benzotriazolyl, cinnolinyl, indazolyl, indolyl, isoquinolinyl, isothiazolyl, naphthyridinyl, purinyl, thienopyridinyl, pyrido[2,3-d]pyrimidinyl, pyrrolo[2,3-b]pyridinyl, quinazolinyl, quinolinyl, thieno[2,3-c]pyridinyl, pyrazolo[3,4-b]pyridinyl, pyrazolo[3,4-c]pyridinyl, pyrazolo[4,3-c]pyridine, pyrazolo[4,3-b]pyridinyl, tetrazolyl, chromane, 2,3-dihydrobenzo[b][1,4]dioxine, benzo[d][1,3]dioxole, 2,3-dihydrobenzofuran, 2,3-dihydrobenzo[b][1,4]oxathiine, and others. In some embodiments, the heteroaryl is selected from thienyl, pyridinyl, furyl, pyrazolyl, imidazolyl, pyranyl, pyrazinyl, and pyrimidinyl.

As used herein, "halo", "halide" or "halogen" is a chloro, bromo, fluoro, or iodo atom radical. In some embodiments, a halo is a chloro, bromo or fluoro. For example, a halide can be fluoro.

As used herein, "haloalkyl" means a hydrocarbon substituent, which is a linear or branched, alkyl, alkenyl or alkynyl substituted with one or more chloro, bromo, fluoro, and/or iodo atom(s). In some embodiments, a haloalkyl is a fluoroalkyls, wherein one or more of the hydrogen atoms have been substituted by fluoro. In some embodiments, haloalkyls are of 1 to about 3 carbons in length (e.g., 1 to about 2 carbons in length or 1 carbon in length). The term "haloalkylene" means a diradical variant of haloalkyl, and such diradicals may act as spacers between radicals, other atoms, or between a ring and another functional group.

As used herein, "heterocyclyl" means a nonaromatic cyclic ring system comprising at least one heteroatom in the ring system backbone. Heterocyclyls may include multiple fused rings. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 5-7 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N or S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, or S. Examples of heterocyclyl include azirinyl, aziridinyl, azetidinyl, oxetanyl, thietanyl, 1,4,2-dithiazolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl, pyrrolidinyl, tetrahydrofuryl, tetrahydropyridinyl, oxazinyl, thiazinyl, thiinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, piperidinyl, pyrazolidinyl imidazolidinyl, thiomorpholinyl, and others. In some embodiments, the heterocyclyl is selected from azetidinyl, morpholinyl, piperazinyl, pyrrolidinyl, and tetrahydropyridinyl.

As used herein, "monocyclic heterocyclyl" means a single nonaromatic cyclic ring comprising at least one heteroatom in the ring system backbone. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 5-7 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N or S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, or S. Examples of heterocyclyl include azirinyl, aziridinyl, azetidinyl, oxetanyl, thietanyl, 1,4,2-dithiazolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl, pyrrolidinyl, tetrahydropyridinyl, oxazinyl, thiazinyl, thiinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, piperidinyl, pyrazolidinyl imidazolidinyl, thiomorpholinyl, and others.

The term "substituted" refers to moieties having substituents replacing a hydrogen on one or more non-hydrogen atoms of the molecule. It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, e.g., which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. Substituents can include, for example, —(C_{1-9}alkyl) optionally substituted with one or more of hydroxyl, —NH_2, —NH(C_{1-3} alkyl), and —N(C_{1-3} alkyl)$_2$; —(C_{1-9}haloalkyl); a halide; a hydroxyl; a carbonyl [such as —C(O)OR, and —C(O)R]; a thiocarbonyl [such as —C(S)OR, —C(O)SR, and —C(S)R]; —(C_{1-9} alkoxyl) optionally substituted with one or more of halide, hydroxyl, —NH_2, —NH(C_{1-3} alkyl), and —N(C_{1-3} alkyl)$_2$; —$OPO(OH)_2$; a phosphonate [such as —$PO(OH)_2$ and —$PO(OR')_2$]; —OPO(OR')R"; —NRR'; —C(O)NRR'; —C(NR)NR'R"; —C(NR')R"; a cyano; a nitro; an azido; —SH; —S—R; —OSO_2(OR); a sulfonate [such as —SO_2(OH) and —SO_2(OR)]; —SO_2NR'R"; and —SO_2R; in which each occurrence of R, R' and R" are independently selected from H; —(C_{1-9}alkyl); C_{6-10} aryl optionally substituted with from 1-3R'"; 5-10 membered heteroaryl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with from 1-3 R'"; C_{3-7}carbocyclyl optionally substituted with from 1-3 R'"; and 3-8 membered heterocyclyl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with from 1-3 R'"; wherein each R'" is independently selected from —(C_{1-6} alkyl), —(C_{1-6}haloalkyl), a halide (e.g., F), a hydroxyl, —C(O)OR, —C(O)R, —(C_{1-6}alkoxyl), —NRR', —C(O)NRR', and a cyano, in which each occurrence of R and R' is independently selected from H and —(C_{1-6} alkyl). In some embodiments, the substituent is selected from —(C_{1-6}alkyl), —(C_{1-6}haloalkyl), a halide (e.g., F), a hydroxyl, —C(O)OR, —C(O)R, —(C_{1-6} alkoxyl), —NRR', —C(O)NRR', and a cyano, in which each occurrence of R and R' is independently selected from H and —(C_{1-6}alkyl).

As used herein, when two groups are indicated to be "linked" or "bonded" to form a "ring", it is to be understood that a bond is formed between the two groups and may involve replacement of a hydrogen atom on one or both groups with the bond, thereby forming a carbocyclyl, heterocyclyl, aryl, or heteroaryl ring. The skilled artisan will recognize that such rings can and are readily formed by routine chemical reactions. In some embodiments, such rings have from 3-7 members, for example, 5 or 6 members.

The skilled artisan will recognize that some structures described herein may be resonance forms or tautomers of compounds that may be fairly represented by other chemical structures, even when kinetically, the artisan recognizes that such structures are only a very small portion of a sample of such compound(s). Such compounds are clearly contemplated within the scope of this disclosure, though such resonance forms or tautomers are not represented herein.

The compounds provided herein may encompass various stereochemical forms. The compounds also encompass diastereomers as well as optical isomers, e.g., mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art. Unless otherwise indicated, when a disclosed compound is named or depicted by a structure without specifying the stereochemistry and has one or more chiral centers, it is understood to represent all possible stereoisomers of the compound.

The term "administration" or "administering" refers to a method of providing a dosage of a compound or pharmaceutical composition to a vertebrate or invertebrate, including a mammal, a bird, a fish, or an amphibian, where the method is, e.g., orally, subcutaneously, intravenously, intralymphatic, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonarilly, vaginally, rectally, ontologically, neuro-otologically, intraocularly, subconjuctivally, via anterior eye chamber injection, intravitreally, intraperitoneally, intrathecally, intracystically, intrapleurally, via wound irrigation, intrabuccally, intraabdominally, intra-articularly, intra-aurally, intrabronchially, intracapsularly, intrameningeally, via inhalation, via endotracheal or endobronchial instillation, via direct instillation into pulmonary cavities, intraspinally, intrasynovially, intrathoracically, via thoracostomy irrigation, epidurally, intratympanically, intracisternally, intravascularly, intraventricularly, intraosseously, via irrigation of infected bone, or via application as part of any admixture with a prosthetic device. The method of administration can vary depending on various factors, e.g., the components of the pharmaceutical composition, the site of the disease, the disease involved, and the severity of the disease.

A "diagnostic" as used herein is a compound, method, system, or device that assists in the identification or characterization of a health or disease state. The diagnostic can be used in standard assays as is known in the art.

The term "mammal" is used in its usual biological sense. Thus, it specifically includes humans, cattle, horses, monkeys, dogs, cats, mice, rats, cows, sheep, pigs, goats, and non-human primates, but also includes many other species.

The term "pharmaceutically acceptable carrier", "pharmaceutically acceptable diluent" or "pharmaceutically acceptable excipient" includes any and all solvents, cosolvents, complexing agents, dispersion media, coatings, isotonic and absorption delaying agents and the like which are not biologically or otherwise undesirable. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. In addition, various adjuvants such as are commonly used in the art may be included. These and other such compounds are described in the literature, e.g., in the Merck Index, Merck & Company, Rahway, N.J. Considerations for the inclusion of various components in pharmaceutical compositions are described, e.g., in Gilman et al. (Eds.) (2010); *Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 12th Ed., The McGraw-Hill Companies.*

The term "pharmaceutically acceptable salt" refers to salts that retain the biological effectiveness and properties of the compounds provided herein and, which are not biologically or otherwise undesirable. In many cases, the compounds provided herein are capable of forming acid and/or base salts by virtue of the presence of amino and/or carboxyl groups or groups similar thereto. Many such salts are known in the art, for example, as described in WO 87/05297. Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids. Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phos-

phoric acid, and the like. Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases. Inorganic bases from which salts can be derived include, for example, sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum, and the like; particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like, specifically such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

"Solvate" refers to the compound formed by the interaction of a solvent and a compound as provided herein or a salt thereof. Suitable solvates are pharmaceutically acceptable solvates including hydrates.

"Patient" as used herein, means a human or a non-human mammal, e.g., a dog, a cat, a mouse, a rat, a cow, a sheep, a pig, a goat, a non-human primate, or a bird, e.g., a chicken, as well as any other vertebrate or invertebrate. In some embodiments, the patient is a human.

A "therapeutically effective amount" or "pharmaceutically effective amount" of a compound as provided herein is one which is sufficient to achieve the desired physiological effect and may vary according to the nature and severity of the disease condition, and the potency of the compound. "Therapeutically effective amount" is also intended to include one or more of the compounds of Formula I in combination with one or more other agents that are effective to treat the diseases and/or conditions described herein. The combination of compounds can be a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Advances in Enzyme Regulation* (1984), 22, 27-55, occurs when the effect of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the compounds. It will be appreciated that different concentrations may be employed for prophylaxis than for treatment of an active disease. This amount can further depend upon the patient's height, weight, sex, age and medical history.

A therapeutic effect relieves, to some extent, one or more of the symptoms of the disease.

"Treat," "treatment," or "treating," as used herein refers to administering a compound or pharmaceutical composition as provided herein for therapeutic purposes. The term "therapeutic treatment" refers to administering treatment to a patient already suffering from a disease thus causing a therapeutically beneficial effect, such as ameliorating existing symptoms, ameliorating the underlying metabolic causes of symptoms, postponing or preventing the further development of a disorder, and/or reducing the severity of symptoms that will or are expected to develop.

"Drug-eluting" and/or controlled release as used herein refers to any and all mechanisms, e.g., diffusion, migration, permeation, and/or desorption by which the drug(s) incorporated in the drug-eluting material pass therefrom over time into the surrounding body tissue.

"Drug-eluting material" and/or controlled release material as used herein refers to any natural, synthetic or semi-synthetic material capable of acquiring and retaining a desired shape or configuration and into which one or more drugs can be incorporated and from which incorporated drug(s) are capable of eluting over time.

"Elutable drug" as used herein refers to any drug or combination of drugs having the ability to pass over time from the drug-eluting material in which it is incorporated into the surrounding areas of the body.

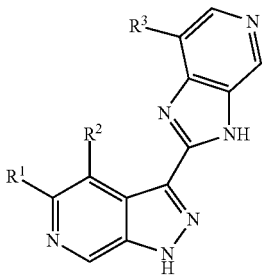
The term "comprising" as used herein is synonymous with "including," "containing," or "characterized by," and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

Compounds

The compounds and compositions described herein can be used as anti-proliferative agents, e.g., anti-cancer and anti-angiogenesis agents, and/or as inhibitors of the Wnt signaling pathway, e.g., for treating diseases or disorders associated with aberrant Wnt signaling.

In addition, the compounds can be used as inhibitors of one or more kinases, kinase receptors, or kinase complexes. Such compounds and compositions are also useful for controlling cellular proliferation, differentiation, and/or apoptosis.

Some embodiments of the present disclosure include compounds of Formula I:



I

or salts, pharmaceutically acceptable salts, or prodrugs thereof.

In some embodiments, R^1 is selected from the group consisting of -pyridinyl(R^4) and -pyrimidinyl(R^5).

In some embodiments, R^1 is selected from the group consisting of -heteroaryl$(R^4)_q$ and -heterocyclyl$(R^5)_h$.

In some embodiments, R^1 is selected from the group consisting of -piperidinyl$(R^5)_h$ and -tetrahydropyridinyl $(R^5)_h$.

In some embodiments, R^1 is selected from the group consisting of -pyridinyl$(R^4)_q$, -pyrimidinyl$(R^4)_q$, -pyrazinyl $(R^4)_q$, -pyrazolyl$(R^4)_q$, and -imidazolyl$(R^4)_q$.

In some embodiments, R^2 is selected from the group consisting of H and halide.

In some embodiments, R^3 is selected from the group consisting of -heteroaryl$(R^6)_q$, -heterocyclyl$(R^7)_h$, and -aryl $(R^8)_k$.

In some embodiments, R^3 is selected from the group consisting of H, -heteroaryl$(R^6)_q$, -heterocyclyl$(R^7)_h$, and -aryl$(R^8)_k$.

In some embodiments, R^3 is selected from the group consisting of -pyridinyl$(R^6)_q$, -imidazolyl$(R^6)_q$, -furanyl $(R^6)_q$, -thiophenyl$(R^6)_q$, -piperidinyl$(R^7)_h$, -piperazinyl $(R^7)_h$, and -phenyl$(R^8)_k$.

In some embodiments, R^4 is one substituent attached to the pyridinyl and is independently selected from the group consisting of H, halide, —(C_{1-6}alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^9)$_h$, —(C_{1-4} alkylene)$_p$carbocyclyl(R^{10}), —(C_{1-4} alkylene)$_p$aryl(R^{11})$_k$, —NHC(=O)R^{12}, —$NR^{13}R^{14}$, and —(C_{1-6} alkylene)$NR^{15}R^{16}$.

In some embodiments, each R^4 is one substituent attached to the heteroaryl and is independently selected from the group consisting of halide, —(C_{1-6}alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^9)$_h$, —(C_{1-4}alkylene)$_p$carbocyclyl(R^{10}), —(C_{1-4} alkylene)$_p$aryl(R^{11})$_k$, —NHC(=O)R^{12}, —$NR^{13}R^{14}$, —(C_{1-6}alkylene)$NR^{15}R^{16}$, and —OR^{22}.

In some embodiments, each R^4 is one substituent attached to the heteroaryl and is independently selected from the group consisting of F, -Me, -Et, —(CH_2)heterocyclyl(R^9)$_h$, -heterocyclyl(R^9)$_h$, —(CH_2)carbocyclyl(R^{10}), —(CH_2)aryl(R^{11})$_k$, —NHC(=O)(C_{1-5} alkyl), —NHC(=O)phenyl(R^{19})$_k$, —NHC(=O)(CH_2)phenyl(R^{19})$_k$, —NHC(=O)carbocyclyl(R^{20})$_j$, —NHC(=O)(CH_2)heterocyclyl(R^{21})$_h$, —NH_2, —N(C_{1-3} alkyl)$_2$, —NH(C_{1-4} alkyl), —(CH_2)N(C_{1-3} alkyl)$_2$, —(CH_2)NH(C_{1-4} alkyl), —OH, —O(C_{1-3} alkyl), —Ocarbocyclyl(R^{20})$_j$, —Oheterocyclyl(R^{21})$_h$, —O(CH_2CH_2)heterocyclyl(R^{21})$_h$, —O(CH_2CH_2)N(C_{1-3} alkyl)$_2$, and —O(CH_2)phenyl(R^{19})$_k$.

In some embodiments, R^5 is one substituent attached to the pyrimidinyl and is independently selected from the group consisting of H, halide, —(C_{1-6}alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^9)$_h$, —(C_{1-4} alkylene)$_p$carbocyclyl(R^{10}), —(C_{1-4} alkylene)$_p$aryl(R^{11})$_k$, —NHC(=O)R^{12}, —$NR^{13}R^{14}$, and —(C_{1-6} alkylene)$NR^{15}R^{16}$.

In some embodiments, each R^5 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4}alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of H, —(C_{1-6}alkyl), halide, —CF_3, —OCH_3, —CN, and —C(=O)R^{17}.

In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-6}alkyl), halide, —CF_3, —OCH_3, —CN, and —C(=O)R^{17}.

In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of -Me, -Et, F, —CF_3, —OCH_3, —CN, and —C(=O)(C_{1-3} alkyl).

In some embodiments, each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of H, —(C_{1-6} alkyl), halide, —CF_3, —CN, and —OCH_3.

In some embodiments, each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-6}alkyl), halide, —CF_3, —CN, and —OCH_3.

In some embodiments, each R^8 is one substituent attached to the aryl and is independently selected from the group consisting of H, —(C_{1-6}alkyl), halide, —CF_3, —CN, —OCH_3, —(C_{1-6} alkylene)$_p$$NHSO_2R^{17}$, —$NR^{13}$($C_{1-6}$ alkylene)$NR^{13}R^{14}$, and —(C_{1-6} alkylene)$_p$$NR^{13}R^{14}$.

In some embodiments, each R^8 is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —CN, —OCH_3, —(C_{1-6} alkylene)$_p$$NHSO_2R^{17}$, —$NR^{13}$($C_{1-6}$ alkylene)$NR^{13}R^{14}$, —(C_{1-6} alkylene)$_p$$NR^{13}R^{14}$, and —$OR^{25}$.

In some embodiments, each R^8 is one substituent attached to the aryl and is independently selected from the group consisting of -Me, -Et, F, —CF_3, —CN, —OCH_3, —(CH_2CH_2)$NHSO_2$(C_{1-3} alkyl), —NH(CH_2CH_2)N(C_{1-3} alkyl)$_2$, —OH, —O(C_{1-3}alkyl), —O(CH_2CH_2)heterocyclyl(R^{21})$_h$, and —O(CH_2CH_2)N(C_{1-3} alkyl)$_2$.

In some embodiments, each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of H, —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, Me, Et, F, Cl, and —CF_3.

In some embodiments, each R^{10} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of H, —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{10} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{10} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

In some embodiments, each R^{11} is one substituent attached to the aryl and is independently selected from the group consisting of H, —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{11} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{11} is one substituent attached to the aryl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

In some embodiments, each R^{12} is independently selected from the group consisting of —(C_{1-9}alkyl), -heteroaryl(R^{18})$_q$, -aryl(R^{19})$_k$, —CH_2aryl(R^{19})$_k$, -carbocyclyl(R^{20})$_j$, and —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, each R^{12} is independently selected from the group consisting of —(C_{1-9}alkyl), -heteroaryl(R^{18})$_q$, -aryl(R^{19})$_k$, —CH_2aryl(R^{19})$_k$, -carbocyclyl(R^{20})$_j$, —CH_2carbocyclyl(R^{20})$_j$, —(C_{1-4} alkylene)$_p$$NR^{23}R^{24}$, -heterocyclyl($R^{21}$)$_h$, and —$CH_2$heterocyclyl($R^{21}$)$_h$.

In some embodiments, each R^{12} is independently selected from the group consisting of —(C_{1-5}alkyl), -phenyl(R^{19})$_k$, —(CH_2)phenyl(R^{19})$_k$, -carbocyclyl(R^{20})$_j$, —(CH_2)carbocyclyl(R^{20})$_j$, —(CH_2)N(C_{1-3} alkyl)$_2$, and —(CH_2)heterocyclyl(R^{21})$_h$.

In some embodiments, each R^{13} is independently selected from the group consisting of H and —(C_{1-6}alkyl).

In some embodiments, each R^{13} is independently selected from the group consisting of H and —(C_{1-3}alkyl).

In some embodiments, each R^{14} is independently selected from the group consisting of H, —(C_{1-6}alkyl), —CH_2aryl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, each R^{14} is independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, each R^{15} is independently selected from the group consisting of H and —(C_{1-6}alkyl).

In some embodiments, each R^{15} is independently selected from the group consisting of H and —(C_{1-3}alkyl).

In some embodiments, each R^{16} is independently selected from the group consisting of H, —(C_{1-6}alkyl), —CH_2aryl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, each R^{16} is independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, each R^{17} is independently a —(C_{1-6} alkyl).

In some embodiments, each R^{17} is independently a —(C_{1-3} alkyl).

In some embodiments, each R^{18} is one substituent attached to the heteroaryl and is independently selected from the group consisting of H, —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{18} is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{18} is one substituent attached to the heteroaryl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

In some embodiments, each R^{19} is one substituent attached to the aryl and is independently selected from the group consisting of H, —(C_{1-4}alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{19} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{19} is one substituent attached to the aryl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

In some embodiments, each R^{20} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of H, —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{20} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{20} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

In some embodiments, each R^{21} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN.

In some embodiments, each R^{21} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

In some embodiments, R^{22} is selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{21})$_h$, —(C_{1-4} alkylene)$_p$carbocyclyl(R^{20})$_j$, —(C_{1-4} alkylene)$_p$aryl(R^{19})$_k$, and —(C_{1-6}alkylene)$_p$$NR^{23}R^{24}$.

In some embodiments, R^{22} is selected from the group consisting of H, -Me, -Et, -iPr, -heterocyclyl(R^{21})$_h$, —(CH_2CH_2)heterocyclyl(R^{21})$_h$, -carbocyclyl(R^{20})$_j$, —(CH_2)phenyl(R^{19})$_k$, and —(CH_2CH_2)N(C_{1-3} alkyl)$_2$.

In some embodiments, each R^{23} is independently selected from the group consisting of H and —(C_{1-6}alkyl).

In some embodiments, each R^{23} is independently selected from the group consisting of Me and Et.

In some embodiments, each R^{24} is independently selected from the group consisting of H and —(C_{1-6}alkyl).

In some embodiments, each R^{24} is independently selected from the group consisting of Me and Et.

In some embodiments, R^{25} is selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{21})$_h$, and —(C_{1-6} alkylene)$_p$$NR^{23}R^{24}$.

In some embodiments, R^{25} is selected from the group consisting of H, -Me, -Et, -iPr, —(CH_2CH_2)heterocyclyl(R^{21})$_h$, and —(CH_2CH_2)N(C_{1-3} alkyl)$_2$.

In some embodiments, each p is independently 0 or 1.

In some embodiments, each q is independently 1 to 4.

In some embodiments, each h is independently 1 to 10.

In some embodiments, each k is independently 1 to 5.

In some embodiments, each j is independently 1 to 12.

In some embodiments, each p is independently 0 or 1; in some embodiments, each p is 0; in some embodiments, each p 1.

In some embodiments, each q is independently 0 to 4; in some embodiments, each q is 0; in some embodiments, each q is 1; in some embodiments, each q is 2; in some embodiments, each q is 3; in some embodiments, each q is 4.

In some embodiments, each h is independently 0 to 10; in some embodiments, each h is 0; in some embodiments, each h is 1; in some embodiments, each h is 2; in some embodiments, each h is 3; in some embodiments, each h is 4.

In some embodiments, each k is independently 0 to 5; in some embodiments, each k is 0; in some embodiments, each k is 1; in some embodiments, each k is 2; in some embodiments, each k is 3.

In some embodiments, each j is independently 0 to 12; in some embodiments, each j is 0; in some embodiments, each j is 1; in some embodiments, each j is 2; in some embodiments, each j is 3; in some embodiments, each j is 4.

In some embodiments, each R^4 is one substituent attached to the heteroaryl and is selected from the group consisting of —(C_{1-3} alkyl), —CH_2heterocyclyl(R^9)$_h$, —NHC(=O)R^{12}, —$NR^{13}R^{14}$, and —$CH_2NR^{15}R^{16}$.

In some embodiments, at least one R^9 is halide.

In some embodiments, R^{12} is selected from the group consisting of —(C_{1-5} alkyl), -phenyl(R^{19})$_k$, —CH_2phenyl (R^{19})$_k$, and -carbocyclyl(R^{20})$_j$.

In some embodiments, R^{13} and R^{14} are independently selected from H and —(C_{1-5} alkyl).

In some embodiments, R^{15} and R^{16} are independently selected from H and —(C_{1-5} alkyl).

In some embodiments, k is 1 or 2 and each R^8 is independently a halide.

In some embodiments, k is 2, one R^8 is halide and the other R^8 is —$CH_2NHSO_2R^{17}$.

In some embodiments, R^{17} is —(C_{1-3} alkyl).

In some embodiments, k is 2, one R^8 is halide and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$.

In some embodiments, R^{13} and R^{14} are independently selected from H and —(C_{1-3}alkyl).

In some embodiments, R^3 is selected from the group consisting of -pyridinyl(R^6)$_q$, -imidazolyl(R^6)$_q$, -furanyl (R^6)$_q$, and -thiophenyl(R^6)$_q$.

In some embodiments, q is 0 or 1, and R^6 is selected from the group consisting of halide, —(C_{1-3} alkyl), and —C(=O) R^{17}, wherein R^{17} is —(C_{1-2}alkyl).

In some embodiments, R^3 is selected from the group consisting of -piperidinyl(R^7)$_h$ and -piperazinyl(R^7)$_h$.

In some embodiments, q is 1, and R^7 is selected from the group consisting of H and —(C_{1-3} alkyl).

In some embodiments, R^2 is H; in other embodiments, R^2 is halide, e.g. F.

In some embodiments, R^1 is -heteroaryl(R^4)$_q$.

In some embodiments, R^1 is -pyridinyl(R^4)$_q$.

In some embodiments, R^1 is -pyridin-3-yl(R^4)$_q$.

In some embodiments, R^1 is -pyrimidinyl(R^4)$_q$.

In some embodiments, R^1 is -pyrimidin-5-yl(R^4)$_q$.

In some embodiments, R^1 is -pyrimidin-5-yl(R^4)$_q$ and q is 0.

In some embodiments, R^1 is -pyrazinyl$(R^4)_q$.

In some embodiments, R^1 is -pyrazolyl$(R^4)_q$.

In some embodiments, R^1 is -pyrazol-4-yl$(R^4)_q$, q is 1, and R^4 is Me.

In some embodiments, R^1 is -pyrazol-4-yl$(R^4)_q$ and q is 0.

In some embodiments, R^1 is -imidazolyl$(R^4)_q$.

In some embodiments, R^1 is -imidazol-5-yl$(R^4)_q$, q is 1, and R^4 is Me.

In some embodiments, R^1 is -imidazol-5-yl$(R^4)_q$, q is 2, and both R^4 are Me.

In some embodiments, R^1 is -heterocyclyl$(R^5)_h$.

In some embodiments, R^1 is -piperidinyl$(R^5)_h$.

In some embodiments, R^1 is -piperidin-4-yl$(R^5)_h$.

In some embodiments, R^1 is -piperidin-4-yl$(R^5)_h$, and h is 0.

In some embodiments, R^1 is -tetrahydropyridinyl$(R^5)_h$.

In some embodiments, R^1 is -1,2,3,6-tetrahydropyridinyl $(R^5)_h$.

In some embodiments, R^1 is -1,2,3,6-tetrahydropyridinyl $(R^5)_h$, and h is 0.

In some embodiments, R^3 is -heteroaryl$(R^6)_q$.

In some embodiments, R^3 is -heterocyclyl$(R^7)_h$.

In some embodiments, R^3 is -piperidinyl$(R^7)_h$.

In some embodiments, R^3 is -piperazinyl$(R^7)_h$.

In some embodiments, R^3 is -aryl$(R^8)_k$.

In some embodiments, R^3 is -pyridinyl$(R^6)_q$.

In some embodiments, R^3 is -pyridin-3-yl$(R^6)_q$.

In some embodiments, R^3 is -pyridin-4-yl$(R^6)_q$.

In some embodiments, R^3 is -pyridin-5-yl$(R^6)_q$.

In some embodiments, R^3 is -pyridin-3-yl$(R^6)_q$, q is 0.

In some embodiments, R^3 is -pyridin-4-yl$(R^6)_q$, q is 0.

In some embodiments, R^3 is -pyridin-5-yl$(R^6)_q$, q is 0.

In some embodiments, R^3 is -imidazolyl$(R^6)_q$.

In some embodiments, R^3 is -imidazol-1-yl$(R^6)_q$, q is 1, and R^6 is —$(C_{1-3}$ alkyl).

In some embodiments, R^3 is -imidazol-1-yl$(R^6)_q$, q is 1, and R^6 is methyl.

In some embodiments, R^3 is -furanyl$(R^6)_q$.

In some embodiments, R^3 is -furan-2-yl$(R^6)_q$.

In some embodiments, R^3 is -furan-2-yl$(R^6)_q$ and q is 0.

In some embodiments, R^3 is -furan-3-yl$(R^6)_q$.

In some embodiments, R^3 is -furan-3-yl$(R^6)_q$ and q is 0.

In some embodiments, R^3 is -thiophenyl$(R^6)_q$.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$ and q is 0.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and each R^6 is independently a halide.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and R^6 is F.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and each R^6 is independently —$(C_{1-6}$ alkyl).

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and each R^6 is independently —$(C_{1-2}$ alkyl).

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and R^6 is methyl.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and R^6 is —CF_3.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1 or 2, and R^6 is CN.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1, and R^6 is —$C(=O)R^{17}$.

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is —$(C_{1-6}$ alkyl).

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is —$(C_{1-4}$ alkyl).

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is —$(C_{1-2}$ alkyl).

In some embodiments, R^3 is -thiophen-2-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is methyl.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$ and q is 0.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and each R^6 is independently halide.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and R^6 is F.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and each R^6 is independently —$(C_{1-6}$ alkyl).

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and each R^6 is independently —$(C_{1-2}$alkyl).

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and R^6 is methyl.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and R^6 is —CF_3.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1 or 2, and R^6 is CN.

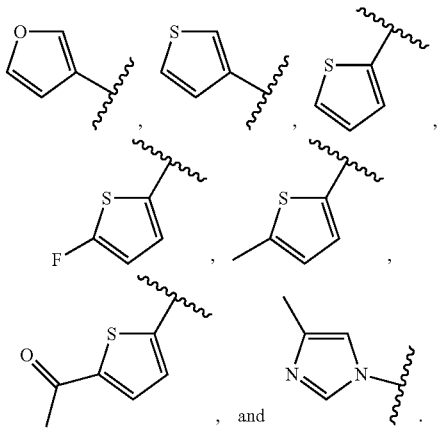
In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1, and R^6 is —$C(=O)R^7$.

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is —$(C_{1-4}$ alkyl).

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is —$(C_{1-2}$ alkyl).

In some embodiments, R^3 is -thiophen-3-yl$(R^6)_q$, q is 1, R^6 is —$C(=O)R^{17}$, and R^{17} is methyl.

In some embodiments, R^3 is selected from the group consisting of:



, and .

In some embodiments, R^3 is -phenyl$(R^8)_k$.

In some embodiments, R^3 is -phenyl$(R^8)_k$ and k is 0.

In some embodiments, R^3 is -phenyl$(R^8)_k$, k is 1 or 2, and each R^8 is independently a halide.

In some embodiments, R^3 is -phenyl$(R^8)_k$, k is 1 or 2, and R^8 is F.

In some embodiments, R^3 is -phenyl$(R^8)_k$, k is 1, and R^8 is F.

In some embodiments, R^3 is -phenyl$(R^8)_k$, k is 2, one R^8 is a halide and the other R^8 is —$(C_{1-6}$alkylene$)_p NHSO_2R^{17}$.

In some embodiments, R^3 is -phenyl$(R^8)_k$, k is 2, one R^8 is a halide and the other R^8 is —$(C_{1-4}$alkylene$)_p NHSO_2R^{17}$, and p is 1.

In some embodiments, R^3 is -phenyl$(R^8)_k$, k is 2, one R^8 is a halide and the other R^8 is —$(C_{1-2}$alkylene$)_p NHSO_2R^{17}$, and p is 1.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is a halide and the other R^8 is —$CH_2NHSO_2R^{17}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is a halide and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is —(C_{1-4}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is a halide and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is a halide and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —NR^{13}(C_{1-6} alkylene)$NR^{13}R^{14}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —NR^{13}(C_{1-5} alkylene)$NR^{13}R^{14}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —NR^{13}(C_{1-4} alkylene)$NR^{13}R^{14}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —NR^{13}(C_{1-3}alkylene)$NR^{13}R^{14}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$NR^{13}CH_2CH_2NR^{13}R^{14}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, R^8 is halide and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from —(C_{1-6}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from —(C_{1-4}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$, and R^{13} and R^{14} are both methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$NHCH_2CH_2NR^{13}R^{14}$, and R^{13} and R^{14} are both methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$OCH_2CH_2NR^{23}R^{24}$.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$OCH_2CH_2NR^{23}R^{24}$, and R^{23} and R^{24} are independently a —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$OCH_2CH_2NR^{23}R^{24}$, and R^{23} and R^{24} are both methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$OCH_2CH_2NR^{23}R^{24}$, and R^{23} and R^{24} are both methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is —(C_{1-4} alkyl).

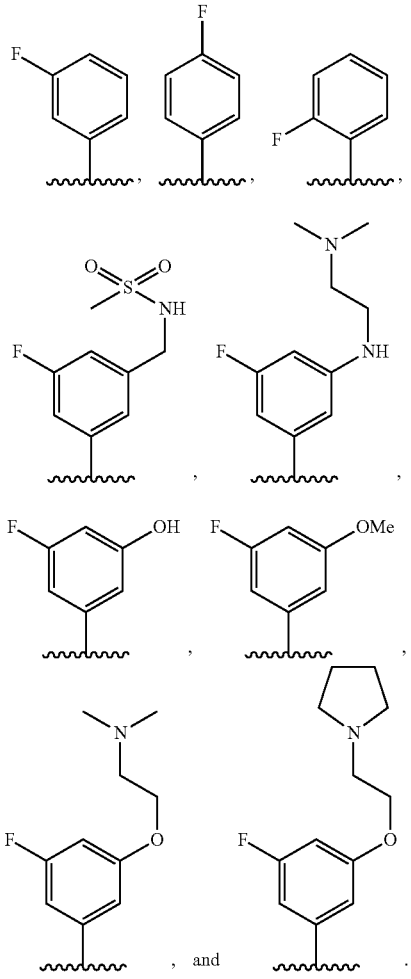
In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is halide and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is methyl.

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is —(C_{1-2}alkyl).

In some embodiments, R^3 is -phenyl(R^8)$_k$, k is 2, one R^8 is F and the other R^8 is —$CH_2NHSO_2R^{17}$, and R^{17} is methyl.

In some embodiments, R^3 is selected from the group consisting of:



In some embodiments, R^3 is -piperidinyl(R^7)$_h$.

In some embodiments, R^3 is -piperidin-1-yl(R^7)$_h$.

In some embodiments, R^3 is -piperidin-1-yl(R^7)$_h$ and h is 0.

In some embodiments, R^3 is -piperidin-1-yl(R^7)$_h$, h is 1 or 2, and each R^7 is independently selected from a halide.

In some embodiments, R^3 is -piperazinyl(R^7)$_h$.

In some embodiments, R^3 is -piperazin-1-yl(R^7)$_h$.

In some embodiments, R^3 is -piperazin-1-yl(R^7)$_h$, h is 1, and R^7 is C_{1-3} alkyl.

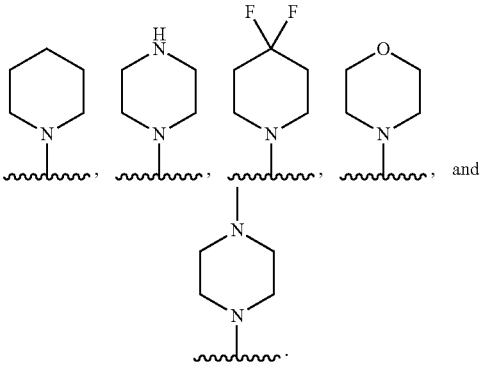
In some embodiments, R^3 is -piperazin-1-yl(R^7)$_h$, h is 1, and R^7 is methyl.

In some embodiments, R^3 is -morpholinyl(R^7)$_h$.

In some embodiments, R^3 is -morpholin-1-yl(R^7)$_h$.

In some embodiments, R^3 is -morpholin-1-yl(R^7)$_h$ and h is 0.

In some embodiments, R^3 is selected from the group consisting of:



In some embodiments, q is 0.

In some embodiments, at least one R^4 is a halide.

In some embodiments, at least one R^4 is a F.

In some embodiments, R^4 is F.

In some embodiments, at least one R^4 is —(C_{1-6}alkyl).

In some embodiments, at least one R^4 is —(C_{1-5}alkyl).

In some embodiments, at least one R^4 is —(C_{1-4}alkyl).

In some embodiments, at least one R^4 is —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —(C_{1-2}alkyl).

In some embodiments, R^4 is a methyl.

In some embodiments, at least one R^4 is —(C_{1-4}alkylene)$_p$ heterocyclyl(R^9)$_h$ and p is 0 or 1.

In some embodiments, at least one R^4 is —(C_{1-3}alkylene)$_p$ heterocyclyl(R^9)$_h$ and p is 0 or 1.

In some embodiments, at least one R^4 is —(C_{1-2}alkylene)$_p$ heterocyclyl(R^9)$_h$ and p is 0 or 1.

In some embodiments, at least one R^4 is —CH_2pyrrolidinyl(R^9)$_h$.

In some embodiments, at least one R^4 is —CH_2pyrrolidinyl(R^9)$_h$ and h is 0.

In some embodiments, R^4 is a —CH_2pyrrolidinyl(R^9)$_h$ and h is 0.

In some embodiments, at least one R^4 is —CH_2pyrrolidinyl(R^9)$_h$, h is 1 or 2, and at least one R^9 is halide.

In some embodiments, at least one R^4 is —CH_2pyrrolidinyl(R^9)$_h$, h is 1 or 2, and at least one R^9 is F.

In some embodiments, R^4 is a —CH_2pyrrolidinyl(R^9)$_h$, h is 1 or 2, and at least one R^9 is halide.

In some embodiments, R^4 is —CH_2pyrrolidinyl(R^9)$_h$, h is 1 or 2, and at least one R^9 is F.

In some embodiments, R^4 is a —CH_2pyrrolidinyl(R^9)$_h$, h is 1 or 2, and each R^9 is F.

In some embodiments, at least one R^4 is —CH_2piperidinyl(R^9)$_h$.

In some embodiments, at least one R^4 is —CH_2piperidinyl(R^9)$_h$ and h is 0.

In some embodiments, R^4 is a —CH_2piperidinyl(R^9)$_h$ and h is 0.

In some embodiments, at least one R^4 is —CH_2piperidinyl(R^9)$_h$ and at least one R^9 is halide.

In some embodiments, at least one R^4 is —CH_2piperidinyl(R^9)$_h$ and at least one R^9 is F.

In some embodiments, at least one R^4 is —CH_2piperidinyl(R^9)$_h$, h is 1 or 2, and at least one R^9 is halide.

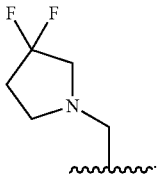
In some embodiments, at least one R^4 is —CH_2piperidinyl(R^9)$_h$, h is 1 or 2, and at least one R^9 is F.

In some embodiments, R^4 is —CH_2piperidinyl(R^9)$_h$, h is 1 or 2, and each R^9 is a halide.

In some embodiments, R^4 is —CH_2piperidinyl(R^9)$_h$, h is 1 or 2, and each R^9 is F.

In some embodiments, R^4 is a —CH_2piperidinyl(R^9)$_h$, h is 1 or 2, and each R^9 is F.

In some embodiments, R^4 is a



In some embodiments, at least one R^4 is —(C_{1-4} alkylene)$_p$ carbocyclyl(R^{10})$_j$.

In some embodiments, at least one R^4 is —(C_{1-4} alkylene)$_p$ carbocyclyl(R^{10})$_j$; and j is 0 or 1.

In some embodiments, at least one R^4 is —(C_{1-3} alkylene)$_p$ carbocyclyl(R^{10})$_j$; and j is 0 or 1.

In some embodiments, at least one R^4 is —(C_{1-2}alkylene)$_p$ carbocyclyl(R^{10})$_j$; and j is 0 or 1.

In some embodiments, at least one R^4 is —CH_2carbocyclyl(R^{10})$_j$.

In some embodiments, R^4 is a —CH_2carbocyclyl(R^{10})$_j$.

In some embodiments, at least one R^4 is —(C_{1-4}alkylene)$_p$ aryl(R^{11})$_k$ and k is 0 or 1.

In some embodiments, at least one R^4 is —(C_{1-3} alkylene)$_p$ aryl(R^{11})$_k$ and k is 0 or 1.

In some embodiments, at least one R^4 is —(C_{1-2}alkylene)$_p$ aryl(R^{11})$_k$ and k is 0 or 1.

In some embodiments, at least one R^4 is —CH_2aryl(R^{11})$_k$.

In some embodiments, at least one R^4 is —CH_2phenyl (R^{11})$_k$.

In some embodiments, R^4 is a —CH_2phenyl(R^{11})$_k$.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}.

In some embodiments, R^4 is a —NHC(=O)R^{12}.

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-9} alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-8} alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-7} alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-6}alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-5}alkyl).

In some embodiments, R^4 is a —NHC(=O)R^{12} and R^{12} is —(C_{1-5}alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-4}alkyl).

In some embodiments, R^4 is a —NHC(=O)R^{12} and R^{12} is —(C_{1-4}alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-3} alkyl).

In some embodiments, R^4 is a —NHC(=O)R^{12} and R^{12} is —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{1-2}alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{2-5}alkyl).

In some embodiments, R^4 is a —NHC(=O)R^{12} and R^{12} is —(C_{2-5}alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —(C_{3-4}alkyl).

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is -aryl(R^{19})$_k$.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is -phenyl(R^{19})$_k$, and k is 0.

In some embodiments, R^4 is a —NHC(=O)R^{12}, R^{12} is -phenyl(R^{19})$_k$, and k is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is —CH_2aryl(R^{19})$_k$.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is —CH_2phenyl(R^{19})$_k$, and k is 0.

In some embodiments, R^4 is —NHC(=O)R^{12}, R^{12} is —CH_2phenyl(R^{19})$_k$, and k is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is -heteroaryl(R^{18})$_q$.

In some embodiments, at least one R^4 is —NHC(=O)R^{12} and R^{12} is -carbocyclyl(R^{20})$_j$.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is -carbocyclyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is -cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHC(=O)R^{12}, R^{12} is -cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is -cyclobutyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHC(=O)R^{12}, R^{12} is -cyclobutyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is -cyclopentyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHC(=O)R^{12}, R^{12} is -cyclopentyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is -cyclohexyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHC(=O)R^{12}, R^{12} is -cyclohexyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is —CH_2carbocyclyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHC(=O)R^{12}, R^{12} is —CH_2cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$.

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from the group consisting of H and —(C_{1-6}alkyl).

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from the group consisting of H and —(C_{1-5}alkyl).

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from the group consisting of H and —(C_{1-4}alkyl).

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from the group consisting of H and —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from the group consisting of H and —(C_{1-2}alkyl).

In some embodiments, at least one R^4 is —$NR^{13}R^{14}$, and R^{13} and R^{14} are independently selected from the group consisting of H and methyl.

In some embodiments, at least one R^4 is —NH_2.

In some embodiments, R^4 is a —NH_2.

In some embodiments, at least one R^4 is —NHR^{14} and R^{14} is —(C_{1-4}alkyl).

In some embodiments, at least one R^4 is —NHR^{14} and R^{14} is —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —NHR^{14} and R^{14} is —(C_{1-2}alkyl).

In some embodiments, R^4 is a —NHR^{14} and R^{14} is —(C_{1-2}alkyl).

In some embodiments, at least one R^4 is —NHR^{14} and R^{14} is —CH_2aryl(R^{19})$_k$.

In some embodiments, at least one R^4 is —NHR^{14}, R^{14} is —CH_2phenyl(R^{19})$_k$, and k is 0.

In some embodiments, R^4 is —NHR^{14}, R^{14} is —CH_2phenyl(R^{19})$_k$, and k is 0.

In some embodiments, at least one R^4 is —NHR^{14} and R^{14} is —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, at least one R^4 is —NHR^{14}, R^{14} is —CH_2cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHR^{14}, R^{14} is —CH_2cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHR^{14}, R^{14} is —CH_2cyclobutyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHR^{14}, R^{14} is —CH_2cyclobutyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHR^{14}, R^{14} is —CH_2cyclopentyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —NHR^{14}, R^{14} is —CH_2cyclopentyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —NHR^{14}, R^{14} is —CH_2cyclohexyl(R^{20}), and j is 0.

In some embodiments, R^4 is a —NHR^{14}, R^{14} is —CH_2cyclohexyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —(C_{1-6}alkylene)$NR^{15}R^{16}$.

In some embodiments, at least one R^4 is —(C_{1-5}alkylene)$NR^{15}R^{16}$.

In some embodiments, at least one R^4 is —(C_{1-4}alkylene)$NR^{15}R^{16}$.

In some embodiments, at least one R^4 is —(C_{1-3} alkylene)$NR^{15}R^{16}$.

In some embodiments, at least one R^4 is —(C_{1-2}alkylene)$NR^{15}R^{16}$.

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$.

In some embodiments, R^4 is a —$CH_2NR^{15}R^{16}$.

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$, and R^5 and R^{16} are independently selected from the group consisting of H and —(C_{1-6}alkyl).

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$, and R^5 and R^{16} are independently selected from the group consisting of H and —(C_{1-5}alkyl).

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-4} alkyl).

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-2}alkyl).

In some embodiments, at least one R^4 is —$CH_2NR^{15}R^{16}$, and R^5 and R^{16} are independently selected from the group consisting of H and methyl.

In some embodiments, R^4 is a —$CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and methyl.

In some embodiments, at least one R^4 is —CH_2NH_2.

In some embodiments, R^4 is a —CH_2NH_2.

In some embodiments, at least one R^4 is —CH_2NMe_2.

In some embodiments, R^4 is —CH_2NMe_2.

In some embodiments, at least one R^4 is —CH_2NHR^{16} and R^{16} is —(C_{1-4} alkyl).

In some embodiments, at least one R^4 is —CH_2NHR^{16} and R^{16} is —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —CH_2NHR^{16} and R^{16} is —(C_{1-2}alkyl).

In some embodiments, R^4 is a —CH_2NHR^{16} and R^{16} is —(C_{1-2}alkyl).

In some embodiments, at least one R^4 is —CH_2NHR^{16} and R^{16} is —CH_2aryl(R^{19})$_k$.

In some embodiments, at least one R^4 is —CH_2NHR^{16}, R^{16} is —CH_2phenyl(R^{19})$_k$, and k is 0.

In some embodiments, R^4 is a —CH_2NHR^{16}, R^{16} is —CH_2phenyl(R^{19})$_k$, and k is 0.

In some embodiments, at least one R^4 is —CH_2NHR^{16} and R^{16} is —CH_2carbocyclyl(R^{20})$_j$.

In some embodiments, at least one R^4 is —CH_2NHR^{16}, R^{16} is —CH_2cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —CH_2NHR^{16}, R^{16} is —CH_2cyclopropyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —CH_2NHR^{16}, R^{16} is —CH_2cyclobutyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —CH_2NHR^{16}, R^{16} is —CH_2cyclobutyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —CH_2NHR^{16}, R^{16} is —CH_2cyclopentyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —CH_2NHR^{16}, R^{16} is —CH_2cyclopentyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —CH_2NHR^{16}, R^{16} is —CH_2cyclohexyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —CH_2NHR^{16}, R^{16} is —CH_2cyclohexyl(R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —OR^{22}.

In some embodiments, at least one R^4 is —OH.

In some embodiments, R^4 is a —OH.

In some embodiments, at least one R^4 is —OR^{22} and R^{22} is —(C_{1-3} alkyl).

In some embodiments, at least one R^4 is —OR^{22} and R^{22} is —(C_{1-2}alkyl).

In some embodiments, at least one R^4 is —OMe.

In some embodiments, R^4 is a —OMe.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is -heterocyclyl(R^{21})$_h$, and h is 0.

In some embodiments, R^4 is a —OR^{22}, R^{22} is -heterocyclyl(R^{21})$_h$, and h is 0.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is -carbocyclyl(R^{20})$_j$, and j is 0.

In some embodiments, R^4 is a —OR^{22}, R^{22} is -carbocyclyl (R^{20})$_j$, and j is 0.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(C_{1-4} alkylene)heterocyclyl(R^{21})$_h$, and h is 0.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(CH_2CH_2)heterocyclyl(R^{21})$_h$, and h is 0.

In some embodiments, R^4 is a —OR^{22}, R^{22} is —(CH_2CH_2)heterocyclyl(R^{21})$_h$, and h is 0.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(C_{1-4} alkylene)$NR^{23}R^{24}$ and R^{23} and R^{24} are independently a —(C_{1-4} alkyl).

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(CH_2CH_2)$NR^{23}R^{24}$ and R^{23} and R^{24} are independently a —(C_{1-2} alkyl).

In some embodiments, at least one R^4 is —OR^{22}, and R^{22} is —(CH_2CH_2)NMe_2.

In some embodiments, R^4 is a —OR^{22}, and R^{22} is —(CH_2CH_2)NMe_2.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(C_{1-4} alkylene)aryl(R^{19})$_k$, k is 0 or 1 and R^{19} is halide.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(CH_2CH_2)phenyl(R^{19})$_k$, k is 0 or 1 and R^{19} is a halide.

In some embodiments, R^4 is a —OR^{22}, R^{22} is —(CH_2CH_2)phenyl(R^{19})$_k$, k is 0 or 1 and R^{19} is a halide.

In some embodiments, at least one R^4 is —OR^{22}, R^{22} is —(CH_2)phenyl(R^{19})$_k$, k is 0 or 1 and R^{19} is a halide.

In some embodiments, R^4 is a —OR^{22}, R^{22} is —(CH_2) phenyl(R^{19})$_k$, k is 0 or 1 and R^{19} is a halide.

In some embodiments, h is 0.

In some embodiments, at least one R^5 is a halide.

In some embodiments, at least one R^5 is a F.

In some embodiments, at least one R^5 is —(C_{1-6} alkyl).

In some embodiments, at least one R^5 is —(C_{1-5}alkyl).

In some embodiments, at least one R^5 is —(C_{1-4} alkyl).

In some embodiments, at least one R^5 is —(C_{1-3} alkyl).

In some embodiments, at least one R^5 is —(C_{1-2} alkyl).

In some embodiments, at least one R^5 is methyl.

In some embodiments, at least one R^6 is a halide.

In some embodiments, at least one R^6 is a F.

In some embodiments, at least one R^6 is —(C_{1-4}alkyl).

In some embodiments, at least one R^6 is —(C_{1-3} alkyl).

In some embodiments, at least one R^6 is —(C_{1-2}alkyl).

In some embodiments, at least one R^6 is methyl.

In some embodiments, R^6 is a methyl.

In some embodiments, at least one R^6 is —C(=O)(C_{1-3} alkyl).

In some embodiments, at least one R^6 is —C(=O)Me.

In some embodiments, R^6 is a —C(=O)Me.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -phenyl(R^8)$_k$; k is 1 or 2; and R^8 is F.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2} alkylene)$_p$$NHSO_2R^{17}$; p is 1; and R^{17} is —(C_{1-3} alkyl).

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)$NR^{13}R^{14}$; and R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl).

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$, wherein q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -heteroaryl(R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -heterocyclyl(R^7)$_h$; h is 1 or 2; and R^7 is selected from the group consisting of halide and —(C_{1-2} alkyl).

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -phenyl(R^8)$_k$; k is 1 or 2; R^8 is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2}alkylene)$_p$$NHSO_2R^{17}$; p is 1; R^{17} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)$NR^{13}R^{14}$; R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl(R^4)$_q$, wherein q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl (R^{20})$_j$; j is 0; R^3 is -heteroaryl(R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl),

and —C(=O)R^{17}; R^{17} is C_{1-3} alkyl; the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl$(R^{20})_j$; j is 0; R^3 is -heterocyclyl$(R^7)_h$; h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2}alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is selected from the group consisting of —$NR^{13}R^{14}$ and —$CH_2NR^{15}R^{16}$; R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$, wherein j and k are 0; R^3 is -phenyl$(R^8)_k$, wherein k is 1 or 2; R^8 is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is selected from the group consisting of —$NR^{13}R^{14}$ and —$CH_2NR^{15}R^{16}$; R^{13}, R^{14}, R^{15}, and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$, wherein k and j are 0; R^3 is -phenyl$(R^8)_k$, wherein k is 2; one R^8 is F and the other R^8 is —(C_{1-2}alkylene)$_p$$NHSO_2R^{17}$; p is 1; R^{17} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is selected from the group consisting of —$NR^{13}R^{14}$ and —$CH_2NR^{15}R^{16}$, wherein R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl), and R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$ wherein k and j are 0; R^3 is -phenyl$(R^8)_k$, wherein k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)$NR^{13}R^{14}$, wherein R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$, wherein q is 1; R^4 is selected from the group consisting of —$NR^{13}R^{14}$ and —$CH_2NR^{15}R^{16}$, wherein R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$, wherein k and j are 0; R^3 is -heteroaryl$(R^6)_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is selected from the group consisting of —$NR^{13}R^{14}$ and —$CH_2NR^{15}R^{16}$; R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$; k and j are 0; R^3 is -heterocyclyl$(R^7)_h$; h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —CH_2heterocyclyl$(R^9)_h$; h is 0-2; R^9 is F; R^3 is -phenyl$(R^8)_k$; k is 1 or 2; R^8 is F; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —CH_2heterocyclyl$(R^9)_h$; h is 0-2; R^9 is F; R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2}alkylene)$_p$$NHSO_2R^{17}$; p is 1; R^{17} is —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —CH_2heterocyclyl$(R^9)_h$; h is 0-2; R^9 is F; R^3 is -phenyl$(R^8)_k$; k is 2; and R^8 is one F and the other R^8—NH(C_{1-6} alkylene)$NR^{13}R^{14}$; R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$, wherein q is 1; R^4 is —CH_2heterocyclyl$(R^9)_h$; h is 0-2; R^9 is F; R^3 is -heteroaryl$(R^6)_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —CH_2heterocyclyl$(R^9)_h$, wherein h is 0-2; R^9 is F; R^3 is -heterocyclyl$(R^7)_h$, wherein h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is H; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -phenyl$(R^8)_k$; k is 1 or 2; and R^8 is F.

In some embodiments, R^2 is H; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2}alkylene)$_p$$NHSO_2R^{17}$; p is 1; and R^{17} is —(C_{1-3} alkyl).

In some embodiments, R^2 is H; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)$NR^{13}R^{14}$; and R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl).

In some embodiments, R^2 is H; R^1 is -pyrimidinyl$(R^4)_q$, wherein q is 0; R^3 is -heteroaryl$(R^6)_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

In some embodiments, R^2 is H; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -heterocyclyl$(R^7)_h$; h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2}alkyl).

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -phenyl$(R^8)_k$; k is 1 or 2; and R^8 is F.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2} alkylene)$_p$$NHSO_2R^{17}$; p is 1; and R^{17} is —(C_{1-3} alkyl).

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)$NR^{13}R^{14}$; and R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl).

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl$(R^4)_q$, wherein q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl);

R^3 is -heteroaryl(R^6)$_q$; wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is —(C_{2-5}alkyl); R^3 is -heterocyclyl(R^7)$_h$; h is 1 or 2; and R^7 is selected from the group consisting of halide and —(C_{1-2} alkyl).

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -phenyl(R^8)$_k$; k is 1 or 2; R^8 is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2}alkylene)$_p$NHSO_2R^{17}; p is 1; R^{17} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)N$R^{13}R^{14}$; R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$, wherein q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -heteroaryl(R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl), and —C(=O)R^{17}; R^{17} is C_{1-3} alkyl; the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —NHC(=O)R^{12}; R^{12} is -carbocyclyl(R^{20})$_j$; j is 0; R^3 is -heterocyclyl(R^7)$_h$; h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2}alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is selected from the group consisting of —N$R^{13}R^{14}$ and —CH_2N$R^{15}R^{16}$; R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$, wherein k and j are 0; R^3 is -phenyl (R^8)$_k$, wherein k is 1 or 2; R^8 is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is selected from the group consisting of —N$R^{13}R^{14}$ and —CH_2N$R^{15}R^{16}$; R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$, wherein k and j are 0; R^3 is -phenyl (R^8)$_k$, wherein k is 2; one R^8 is F and the other R^8 is —(C_{1-2}alkylene)$_p$NHSO_2R^{17}; p is 1; R^{17} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is selected from the group consisting of —N$R^{13}R^{14}$ and —CH_2N$R^{15}R^{16}$, wherein R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl), and R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$, wherein k and j are 0; R^3 is -phenyl (R^8)$_k$, wherein k is 2; one R^8 is F and the other R^8 is —NH(C_{1-6} alkylene)N$R^{13}R^{14}$, wherein R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$, wherein q is 1; R^4 is selected from the group consisting of —N$R^{13}R^{14}$ and —CH_2N$R^{15}R^{16}$; R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$; k and j are 0; R^3 is -heteroaryl (R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is selected from the group consisting of —N$R^{13}R^{14}$ and —CH_2N$R^{15}R^{16}$; R^{13} and R^{15} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{14} and R^{16} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{19})$_k$, and —CH_2carbocyclyl(R^{20})$_j$; k and j are 0; R^3 is -heterocyclyl (R^7)$_h$; h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —CH_2heterocyclyl(R^9)$_h$; h is 0-2; R^9 is F; R^3 is -phenyl(R^8)$_k$; k is 1 or 2; R^8 is F; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —CH_2heterocyclyl(R^9)$_h$; h is 0-2; R^9 is F; R^3 is -phenyl(R^8)$_k$; k is 2; one R^8 is F and the other R^8 is —(C_{1-2} alkylene)$_p$NHSO_2R^{17}; p is 1; R^{17} is —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —CH_2heterocyclyl(R^9)$_h$; h is 0-2; R^9 is F; R^3 is -phenyl(R^8)$_k$; k is 2; and R^8 is one F and the other R^8 is —NH(C_{1-6} alkylene)N$R^{13}R^{14}$; R^{13} and R^{14} are independently selected from —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$, wherein q is 1; R^4 is —CH_2heterocyclyl(R^9)$_h$; h is 0-2; R^9 is F; R^3 is -heteroaryl(R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —(C_{1-2}alkyl), and —C(=O)R^{17}; R^{17} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is F; R^1 is -pyridin-3-yl(R^4)$_q$; q is 1; R^4 is —CH_2heterocyclyl(R^9)$_h$, wherein h is 0-2; R^9 is F; R^3 is -heterocyclyl(R^7)$_h$, wherein h is 1 or 2; R^7 is selected from the group consisting of halide and —(C_{1-2}alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

In some embodiments, R^2 is F; R^1 is -pyrimidinyl(R^4)$_q$ q is 0; R^3 is -phenyl(R^8)$_k$; k is 1 or 2; and R^8 is F.

In some embodiments, R^2 is F; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —$(C_{1-2}$alkylene$)_p NHSO_2R^{17}$; p is 1; and R^{17} is —$(C_{1-3}$ alkyl).

In some embodiments, R^2 is F; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -phenyl$(R^8)_k$; k is 2; one R^8 is F and the other R^8 is —NH$(C_{1-6}$ alkylene$)NR^{13}R^{14}$; and R^{13} and R^{14} are independently selected from —$(C_{1-3}$ alkyl).

In some embodiments, R^2 is F; R^1 is -pyrimidinyl$(R^4)_q$, wherein q is 0; R^3 is -heteroaryl$(R^6)_q$, wherein q is 1; R^6 is selected from the group consisting of halide, —$(C_{1-2}$alkyl), and —C(=O)R^{17}; R^{17} is —$(C_{1-3}$ alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

In some embodiments, R^2 is F; R^1 is -pyrimidinyl$(R^4)_q$; q is 0; R^3 is -heterocyclyl$(R^7)_h$; h is 1 or 2; R^7 is selected from the group consisting of halide and —$(C_{1-2}$alkyl).

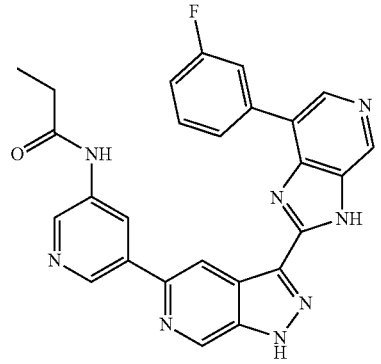
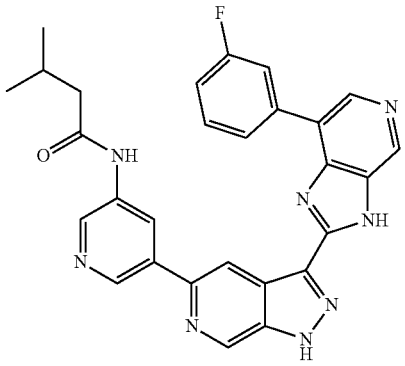
In some embodiments, R^2 is H; R^1 is -pyrazol-4-yl$(R^4)_q$; q is 0 or 1; R^4 is —$(C_{1-3}$ alkyl); R^3 is -phenyl$(R^8)_k$; k is 1 or 2; and R^8 is F.

In some embodiments, R^2 is H; R^1 is -imidazol-5-yl$(R^4)_q$; q is 1 or 2; each R^4 is independently selected from —$(C_{1-3}$ alkyl); R^3 is -phenyl$(R^8)_k$; k is 1 or 2; and R^8 is F.

In some embodiments, R^2 is H; R^1 is -pyridin-3-yl$(R^4)_q$; q is 1; R^4 is —OR^{22}; R^{22} is selected from the group consisting of H and —$(C_{1-3}$ alkyl); R^3 is -phenyl$(R^8)_k$; k is 1 or 2; and R^8 is F.

Illustrative compounds of Formula (I) are shown in Table 1.

TABLE 1

1	
2	

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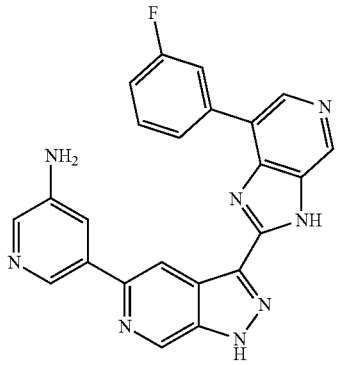
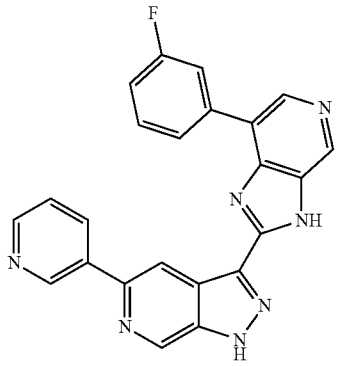
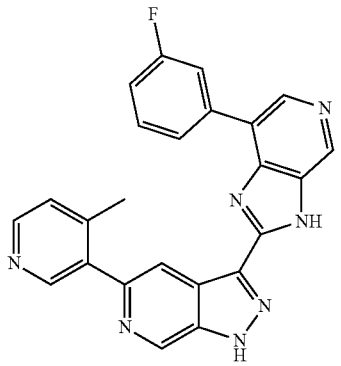
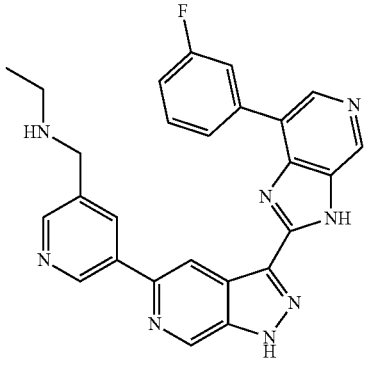
3	
4	
5	
6	

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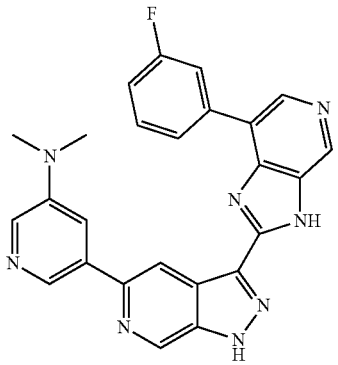
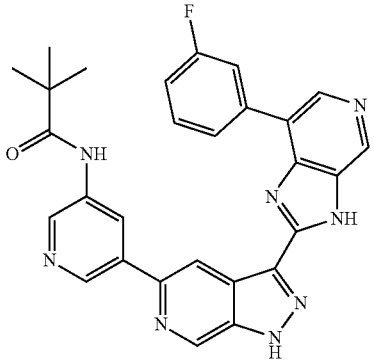
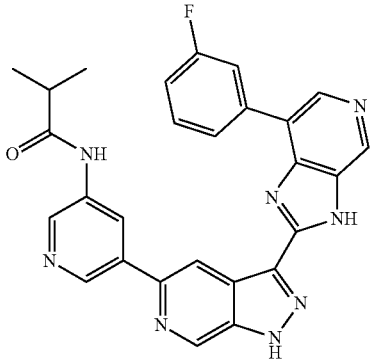
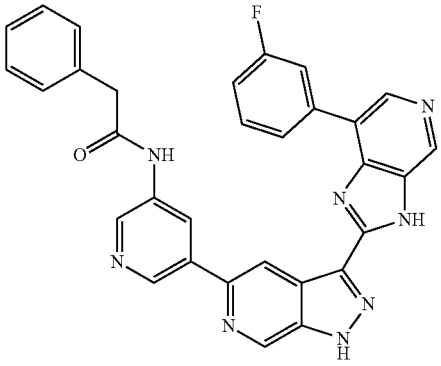
7	
8	
9	
10	

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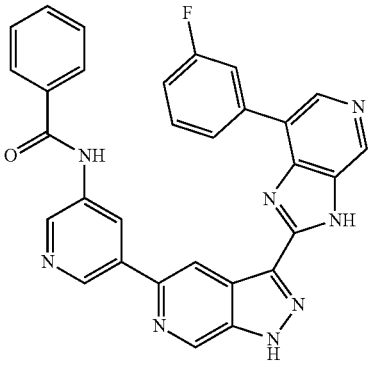
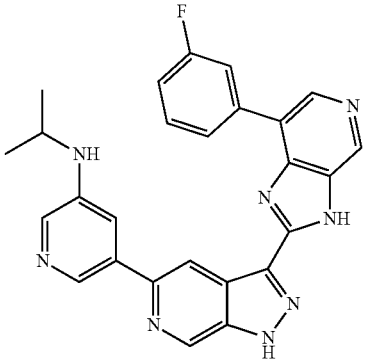
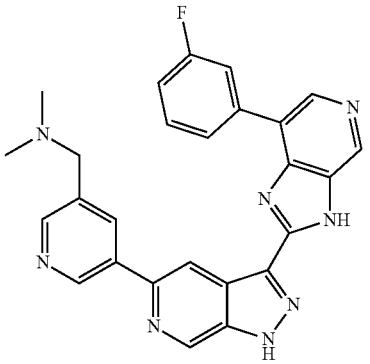
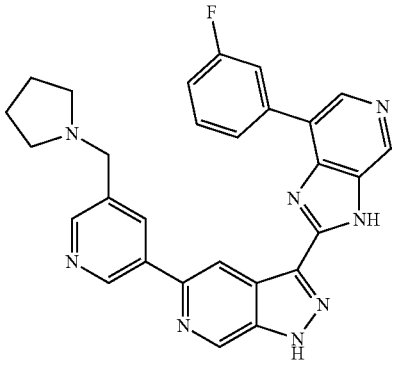
11	
12	
13	
14	

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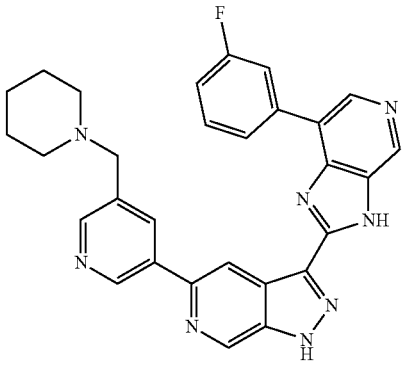
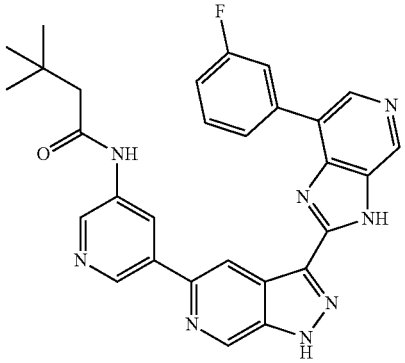
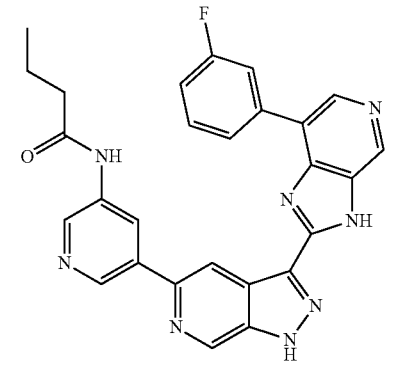
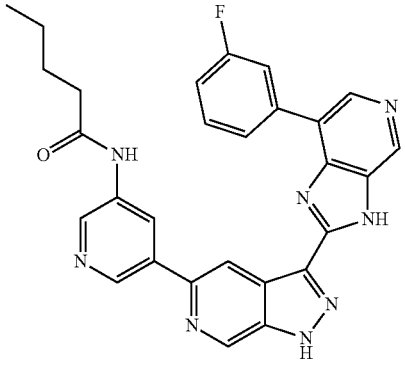
15	
16	
17	
18	

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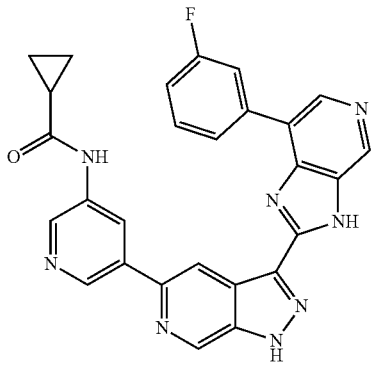
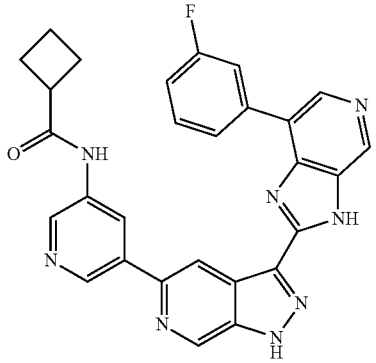
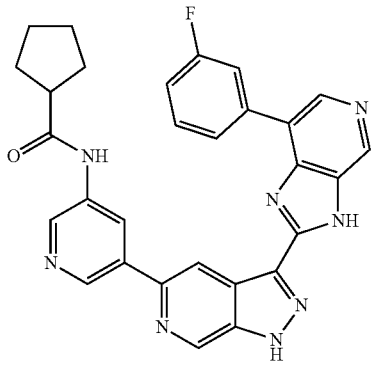
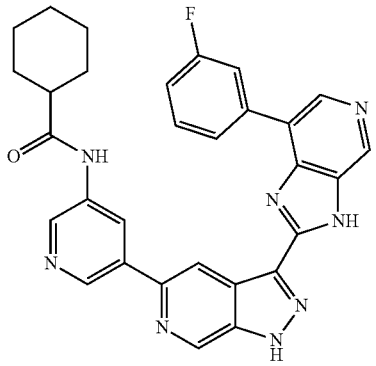
19	
20	
21	
22	

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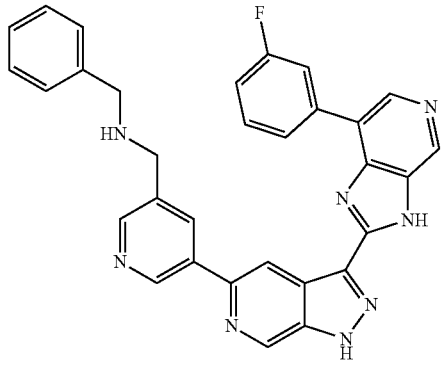
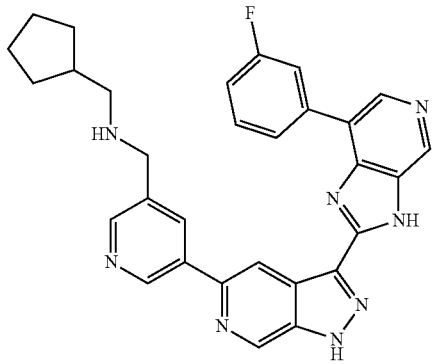
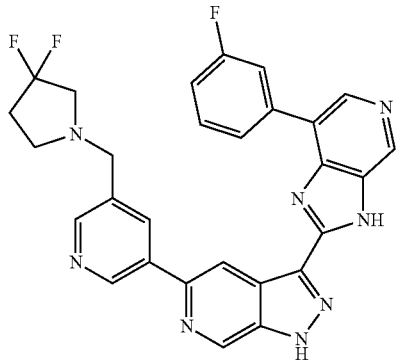
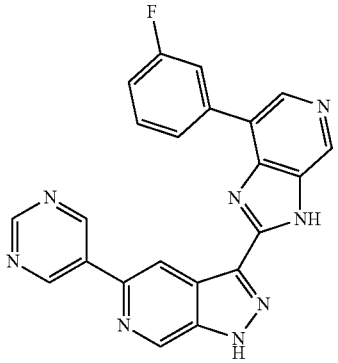
23	
24	
25	
26	

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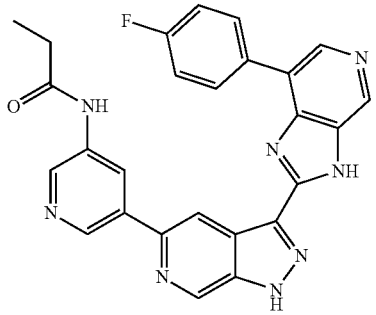
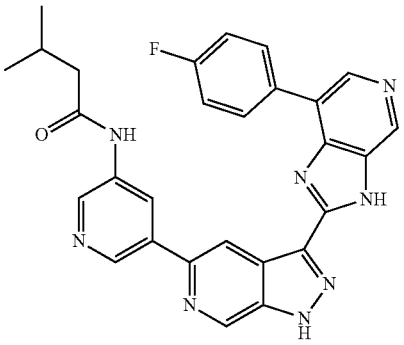
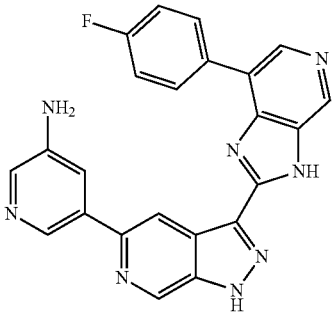
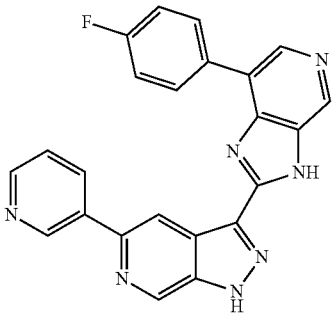
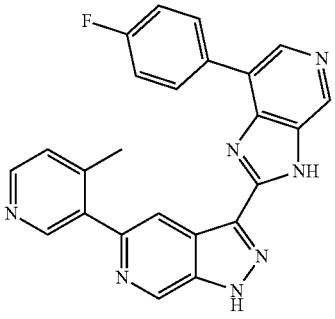
27	
28	
29	
30	
31	

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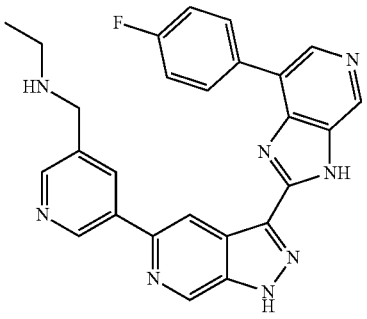
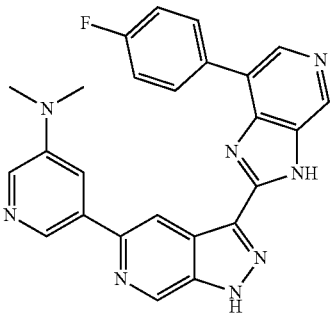
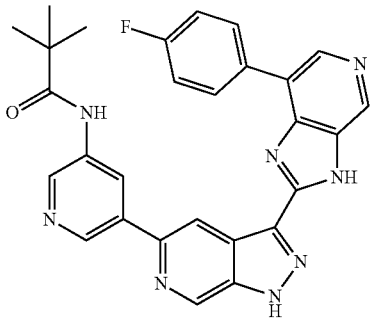
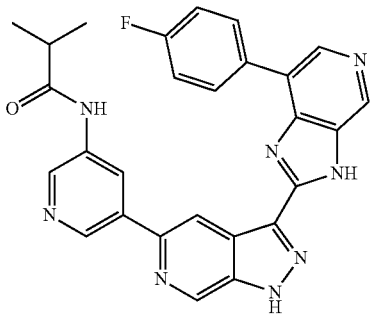
32	
33	
34	
35	

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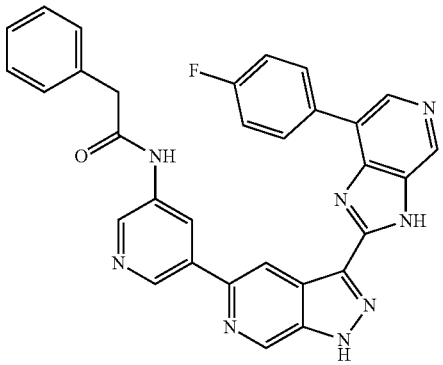
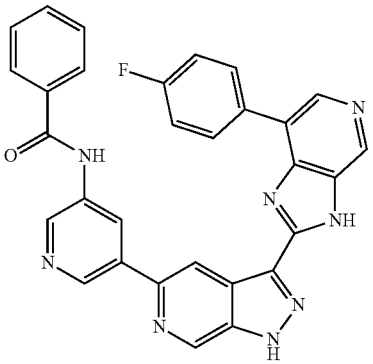
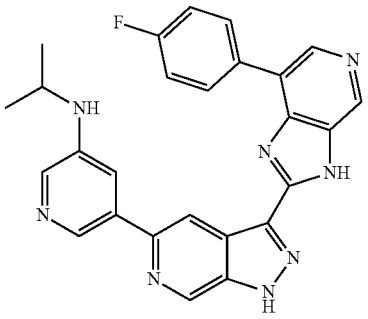
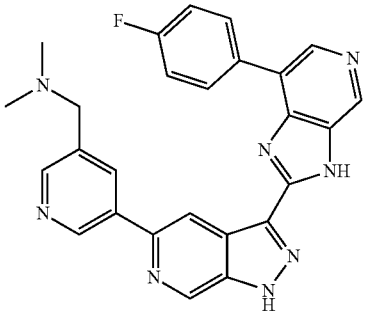
36	
37	
38	
39	

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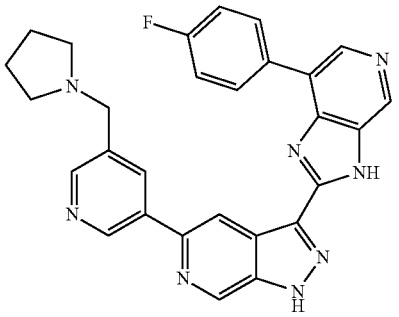
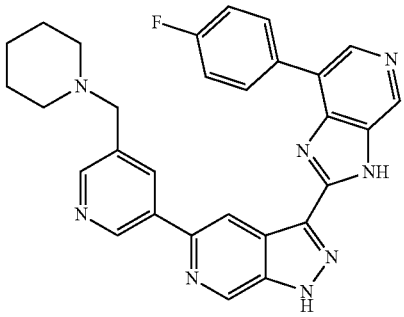
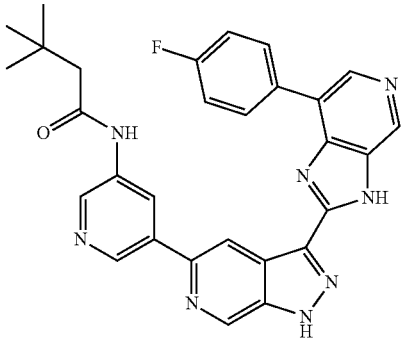
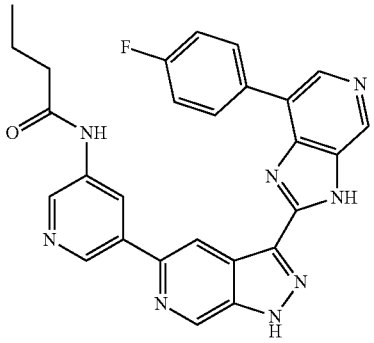
40	
41	
42	
43	

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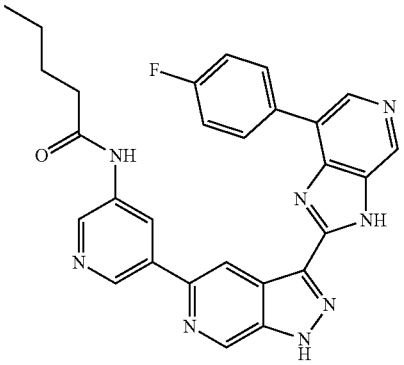
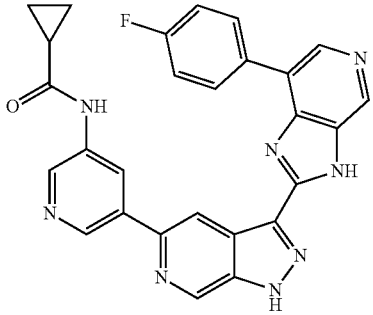
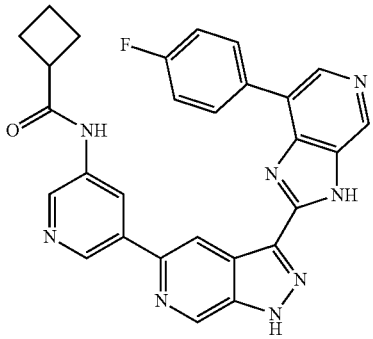
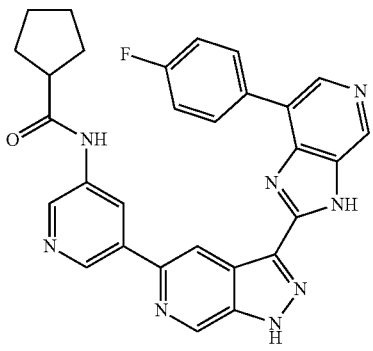
44	
45	
46	
47	

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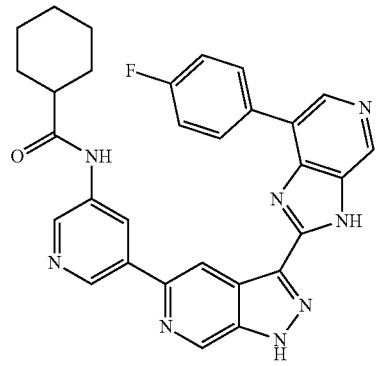
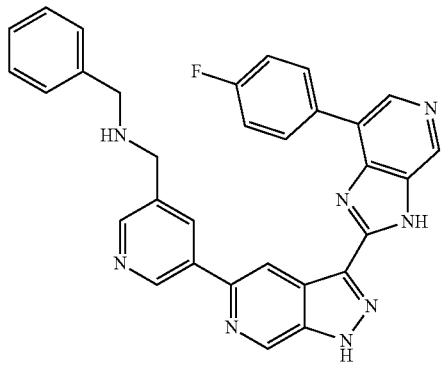
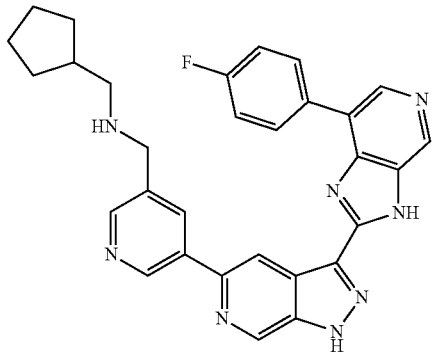
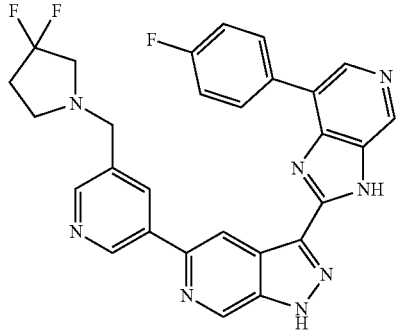
48	
49	
50	
51	

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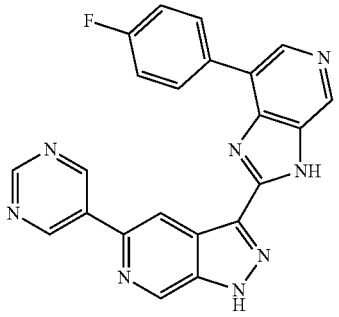
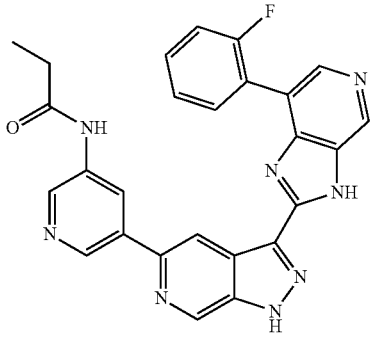
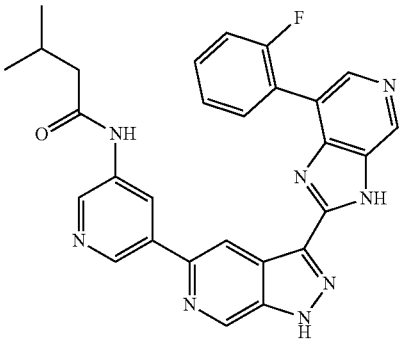
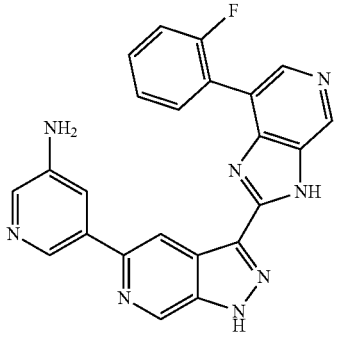
52	
53	
54	
55	

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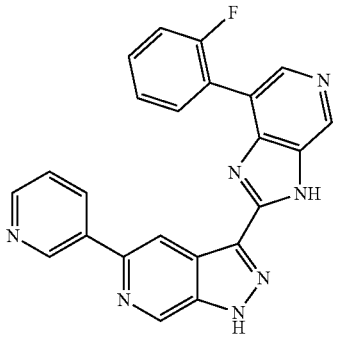
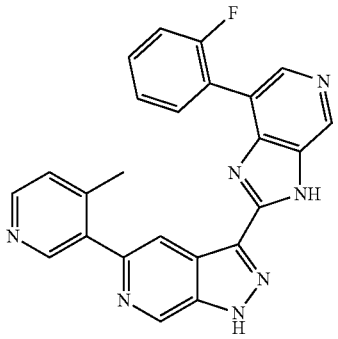
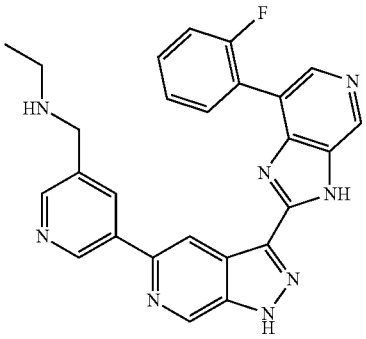
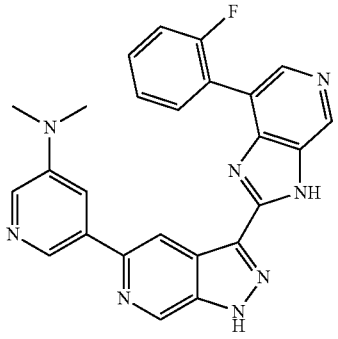
56	
57	
58	
59	

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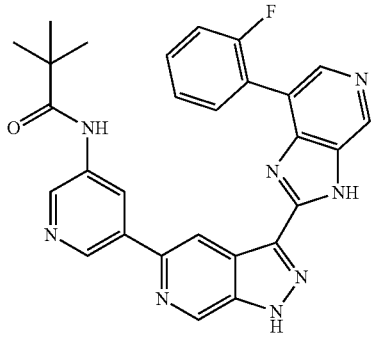
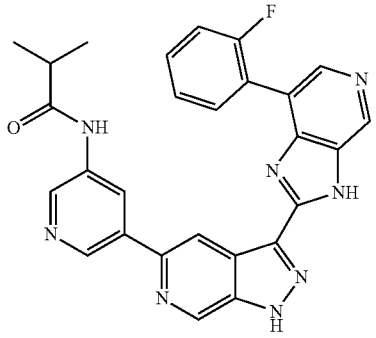
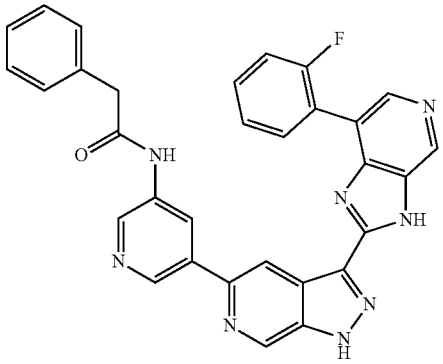
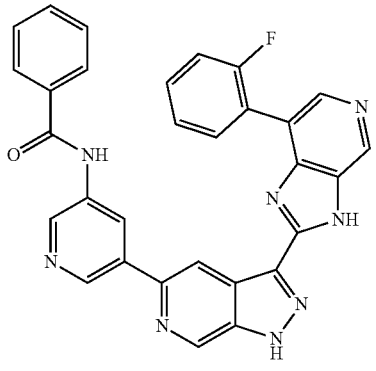
60	
61	
62	
63	

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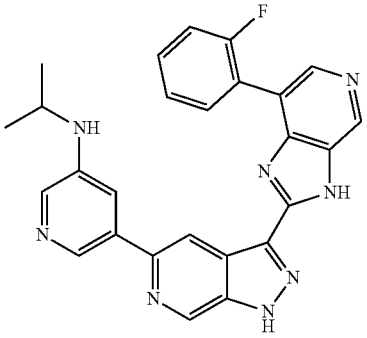
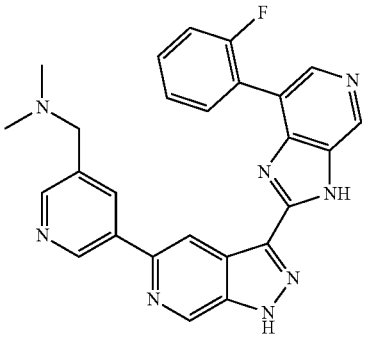
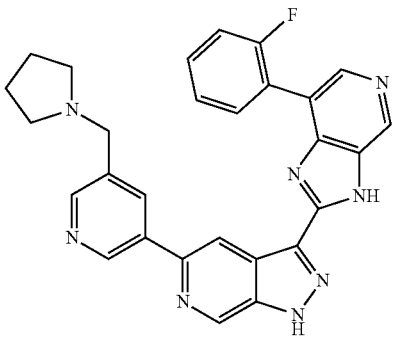
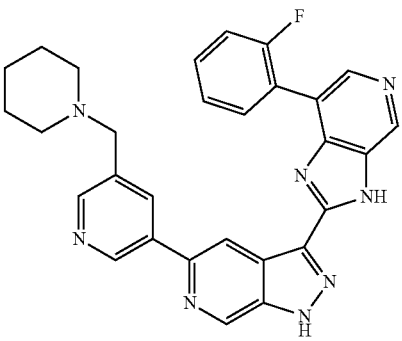
64	
65	
66	
67	

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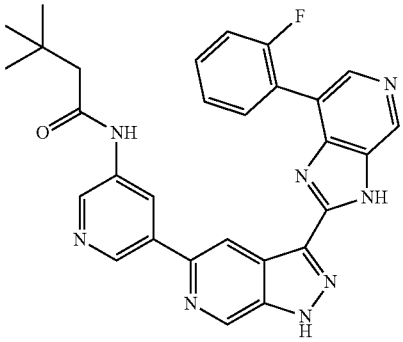
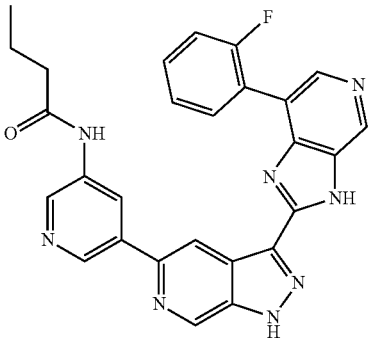
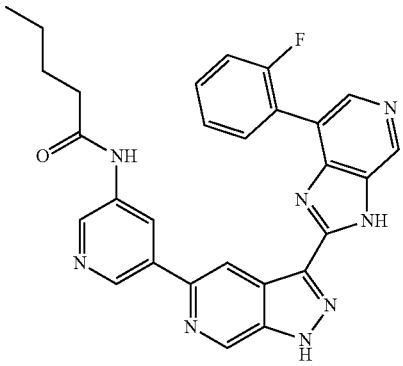
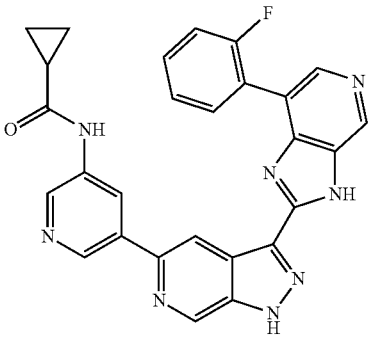
68	
69	
70	
71	

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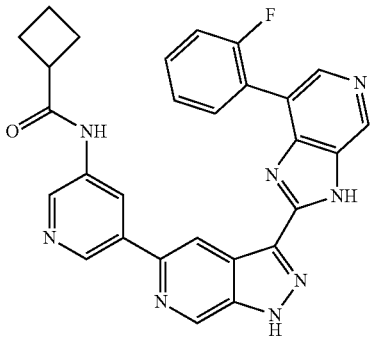
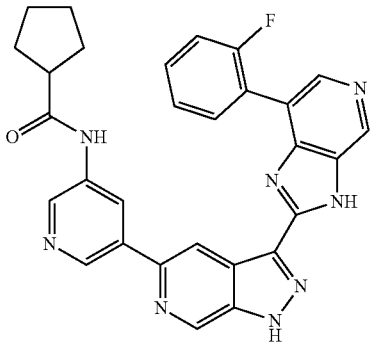
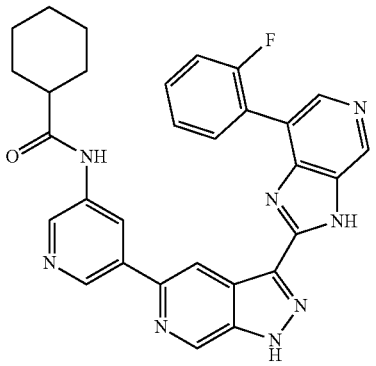
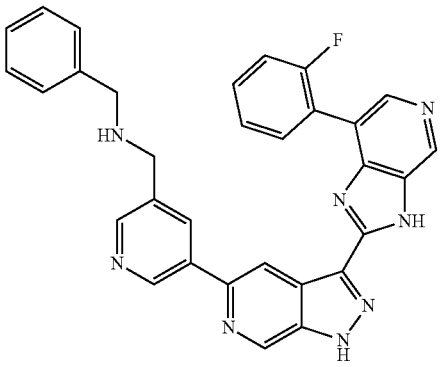
72	
73	
74	
75	

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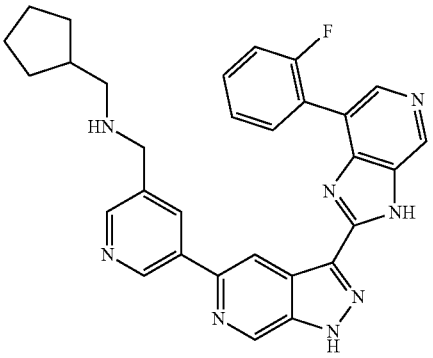
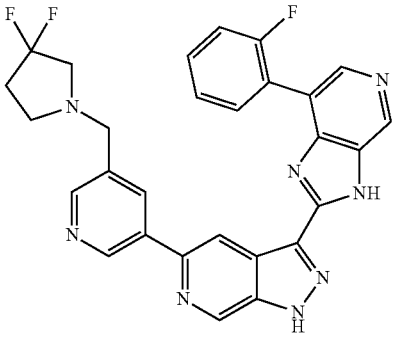
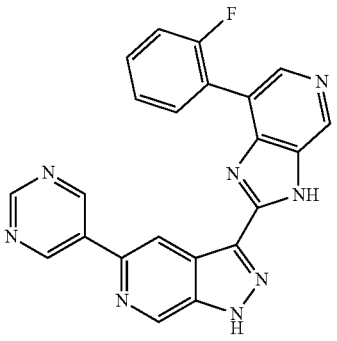
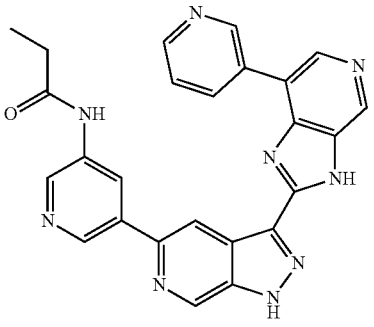
76	
77	
78	
79	

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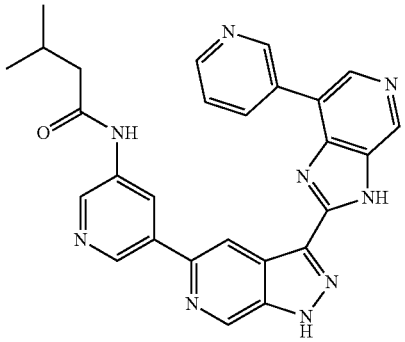
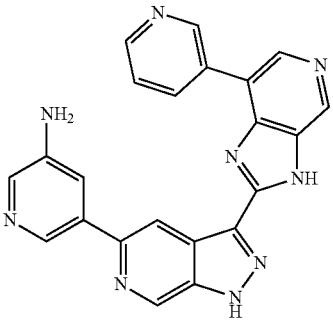
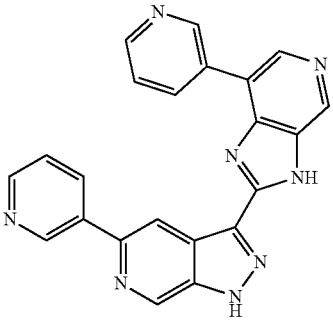
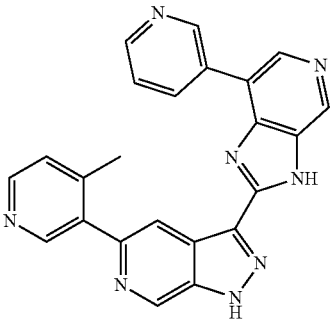
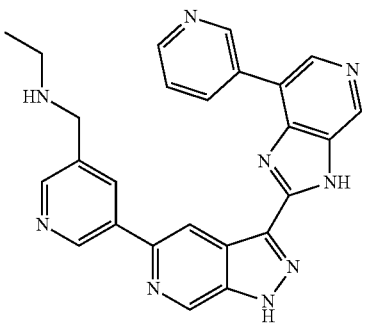
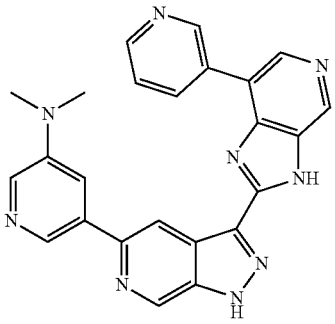
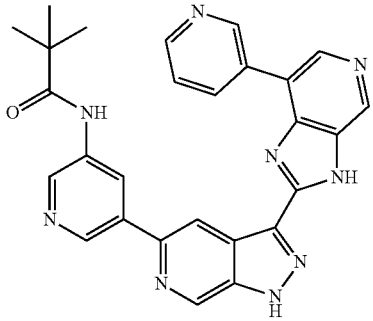
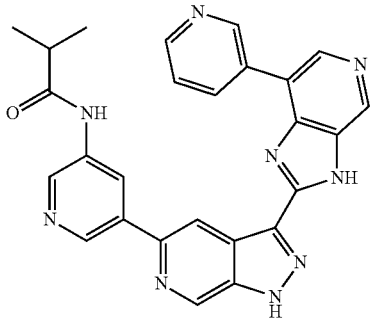
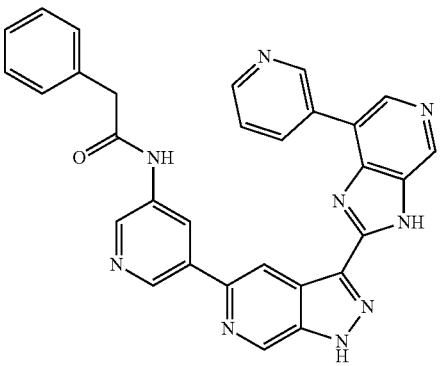
80	
81	
82	
83	
84	

TABLE 1-continued

85	
86	
87	
88	

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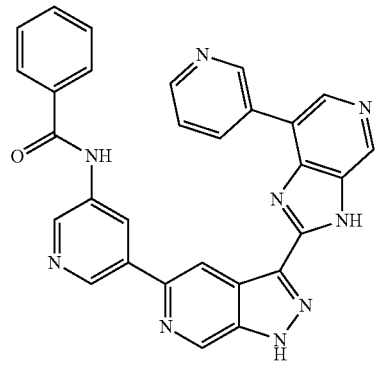
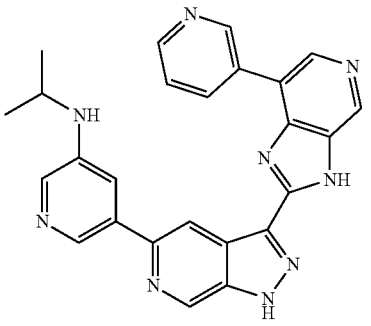
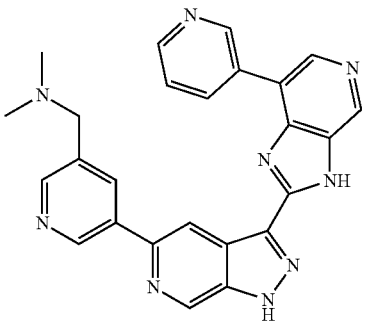
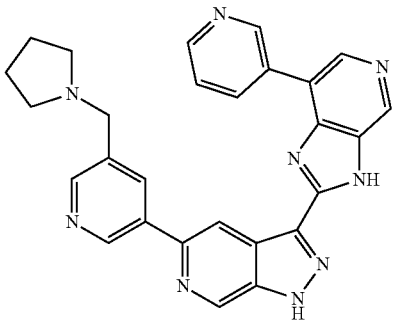
89	
90	
91	
92	

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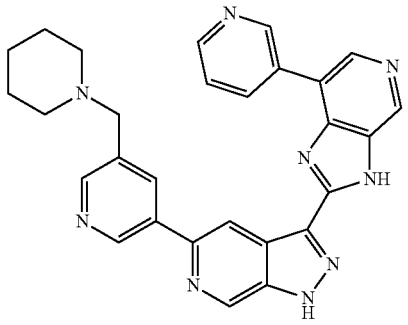
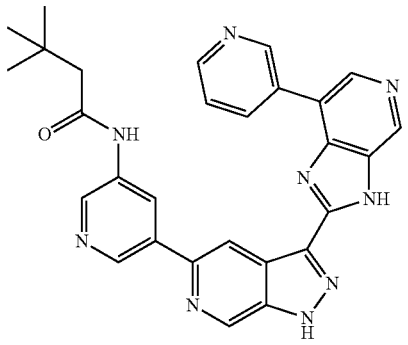
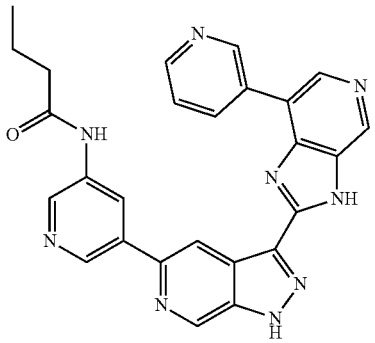
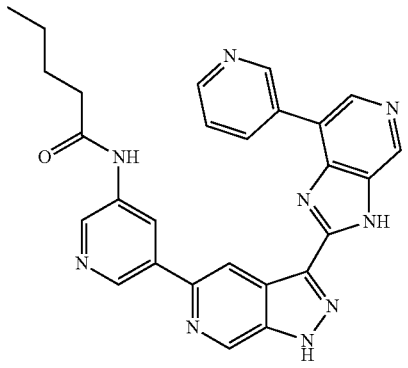
93	
94	
95	
96	

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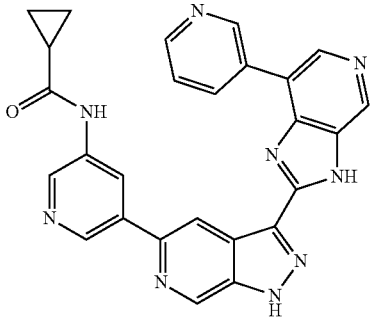
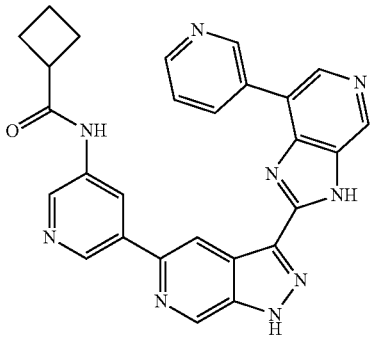
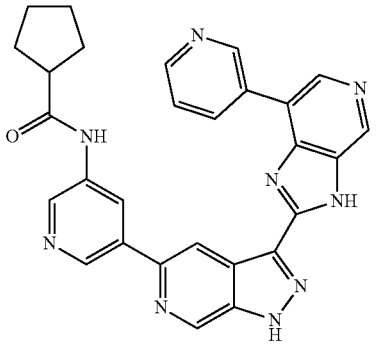
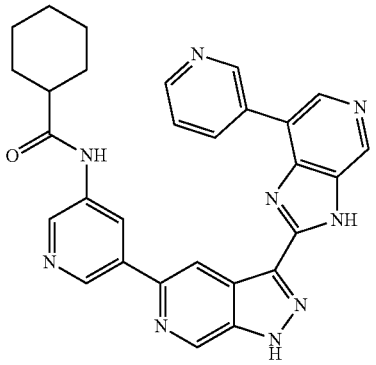
97	
98	
99	
100	

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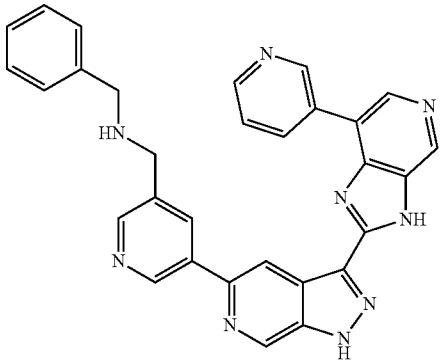
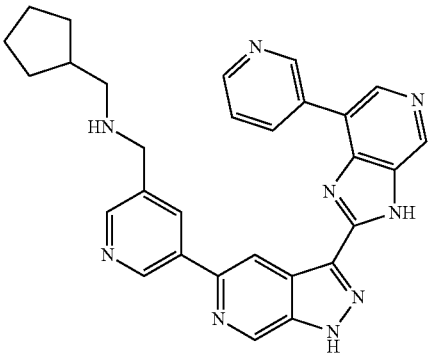
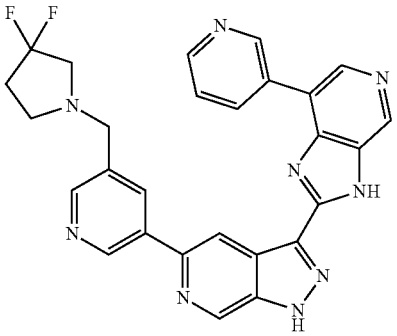
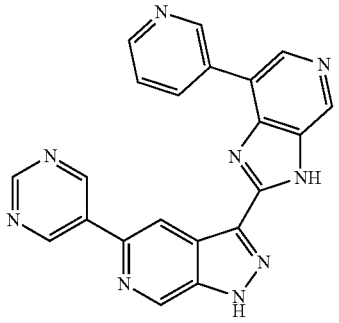
101	
102	
103	
104	

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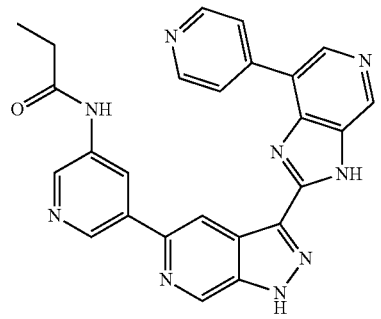
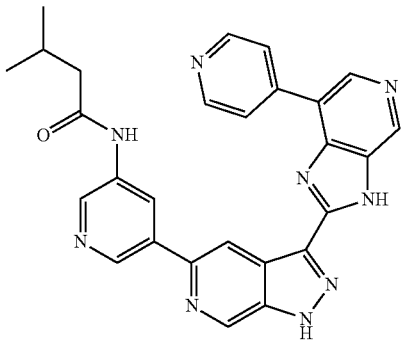
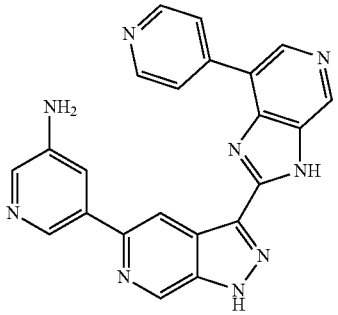
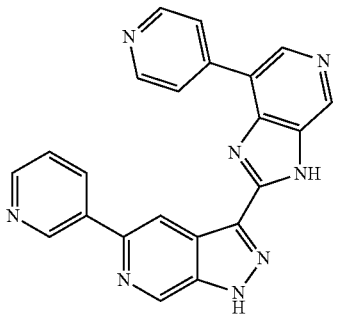
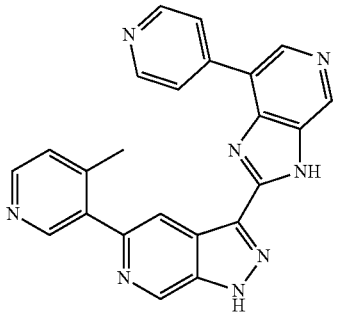
105	
106	
107	
108	
109	

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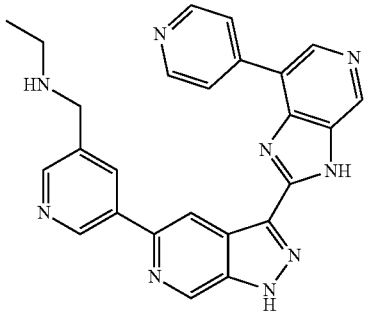
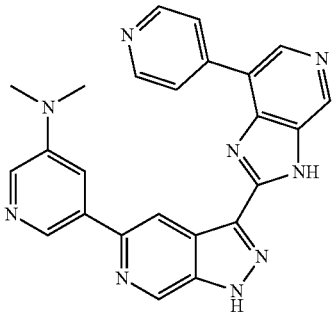
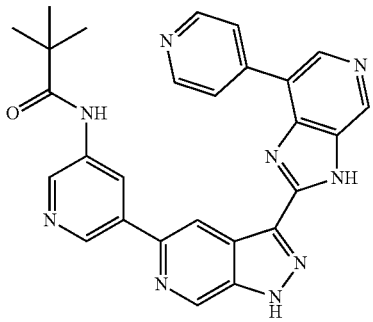
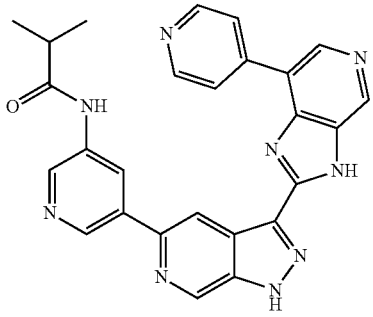
110	
111	
112	
113	

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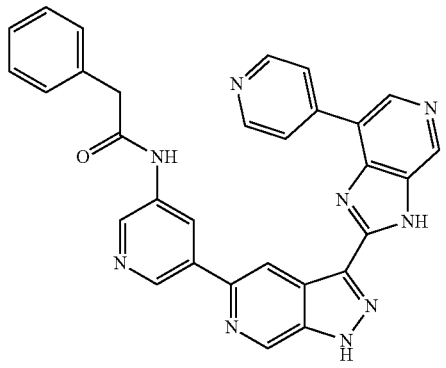
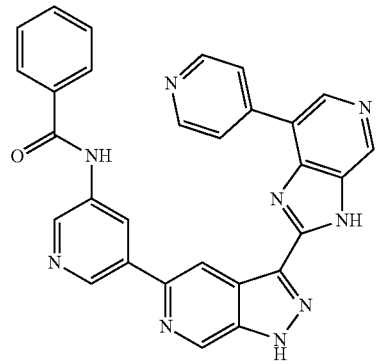
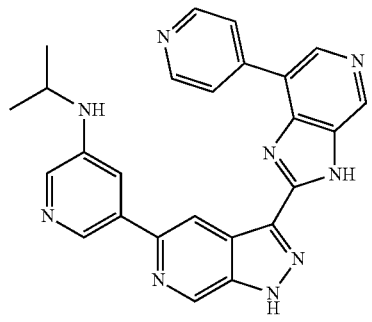
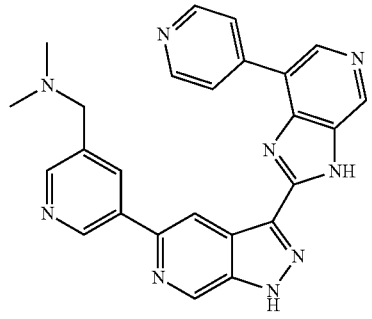
114	
115	
116	
117	

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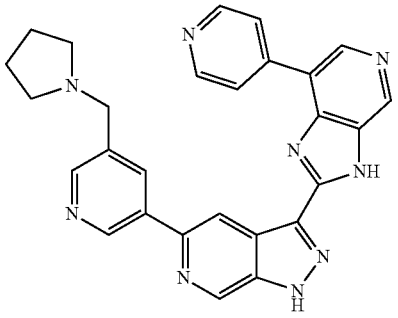
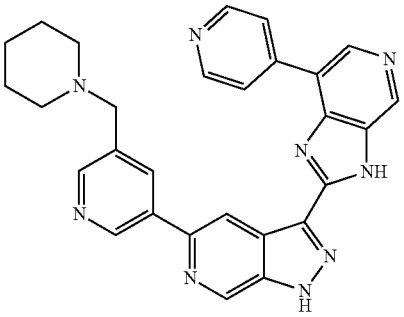
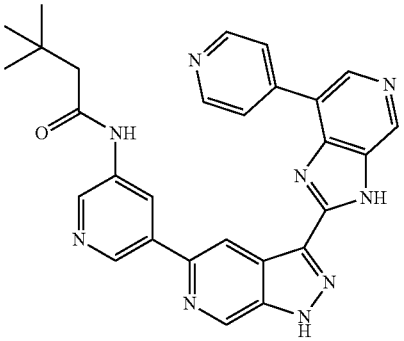
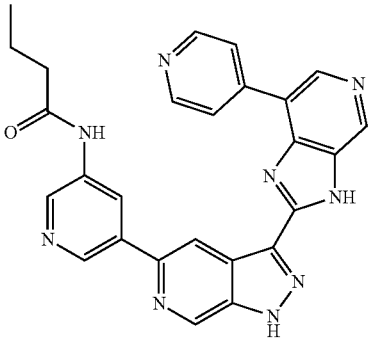
118	
119	
120	
121	

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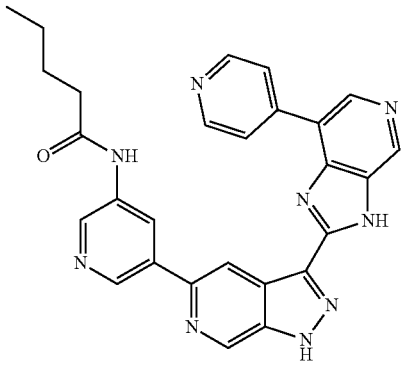
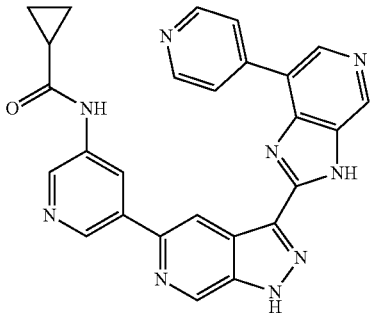
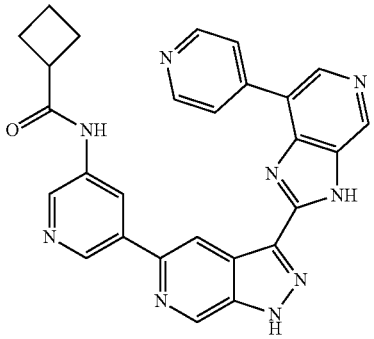
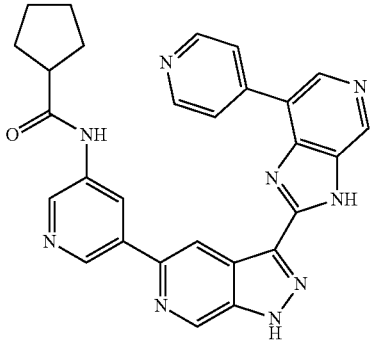
122	
123	
124	
125	

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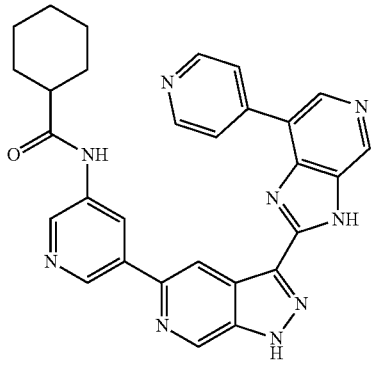
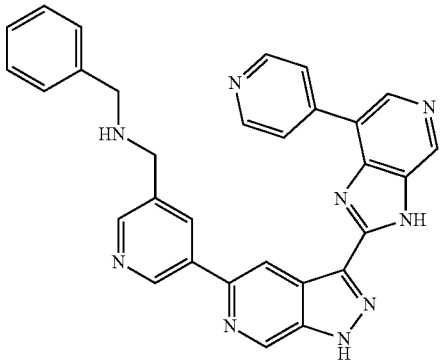
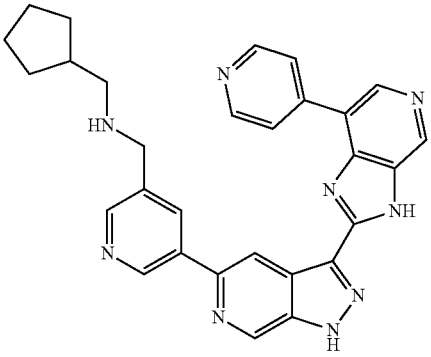
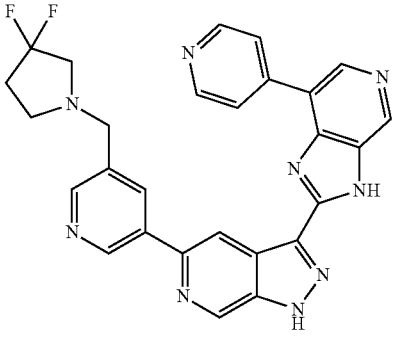
126	
127	
128	
129	

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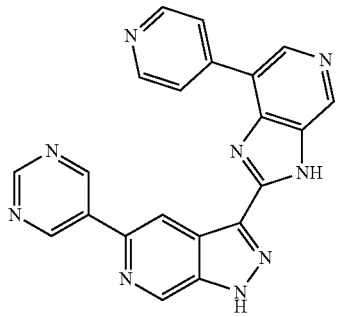
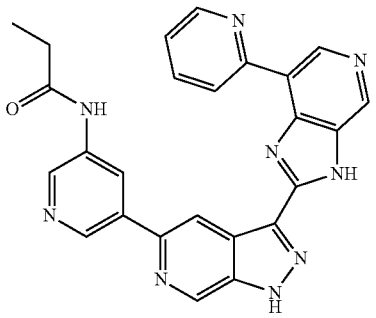
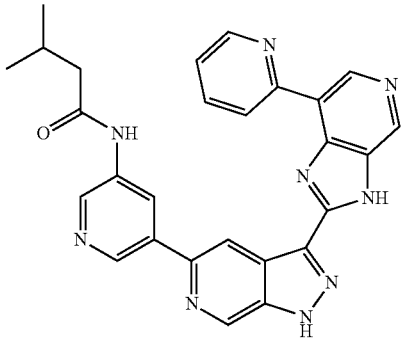
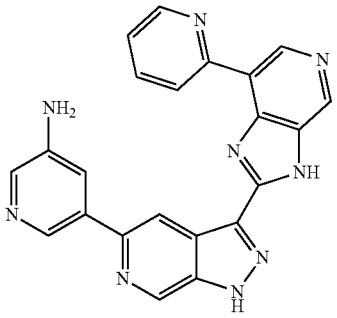
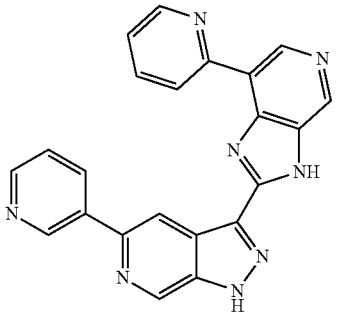
130	
131	
132	
133	
134	

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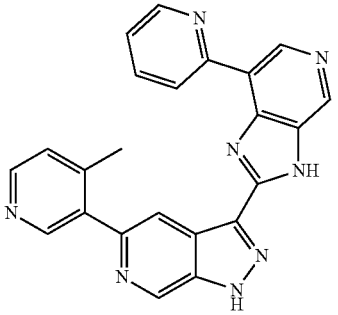
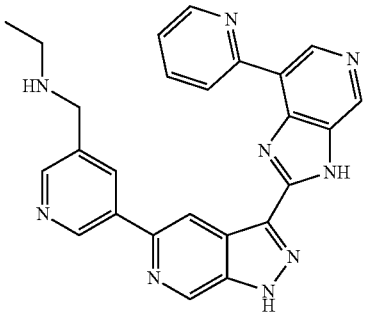
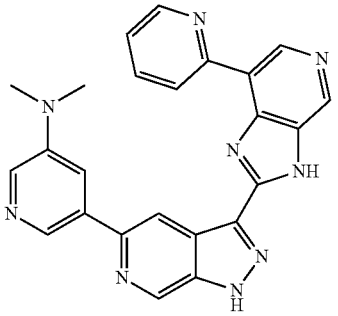
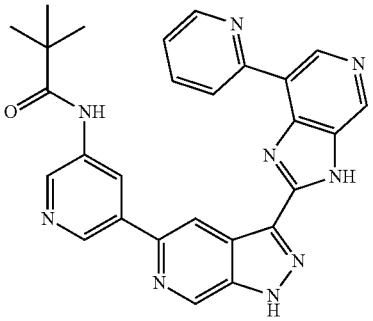
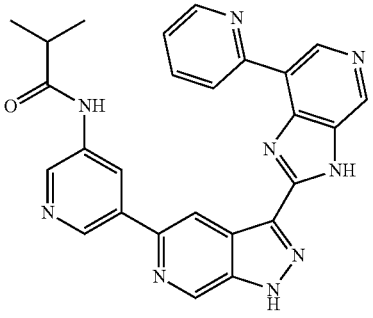
135	
136	
137	
138	
139	

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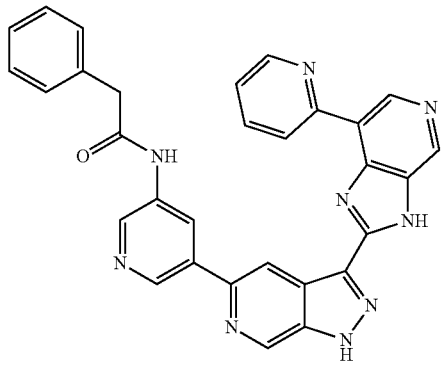
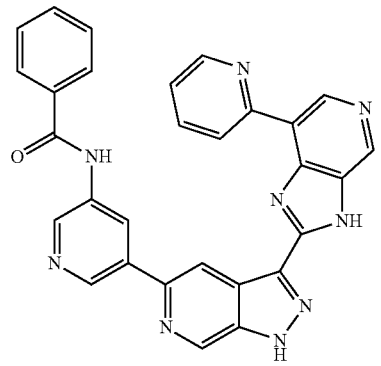
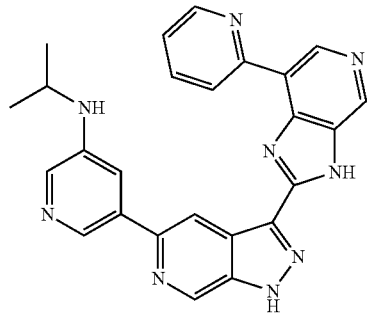
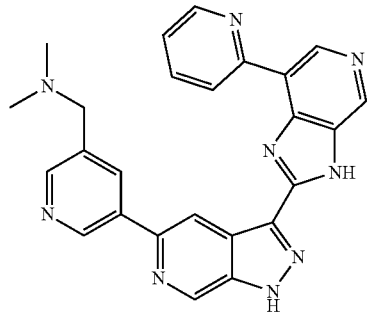
140	
141	
142	
143	

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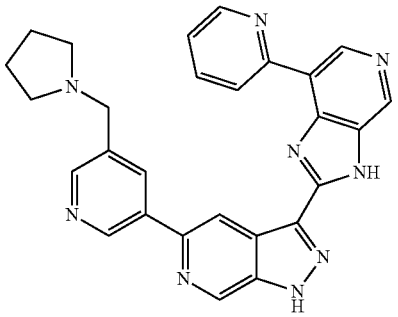
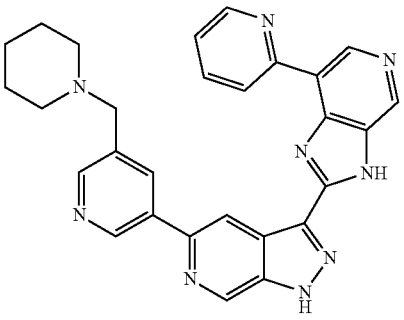
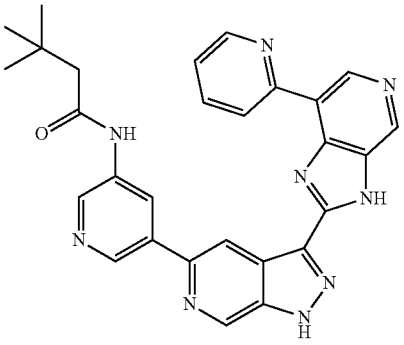
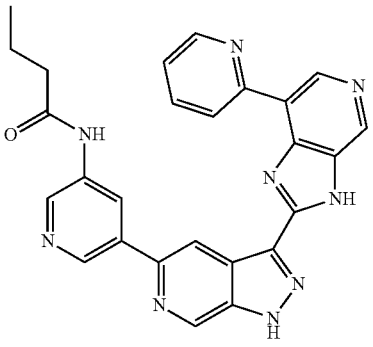
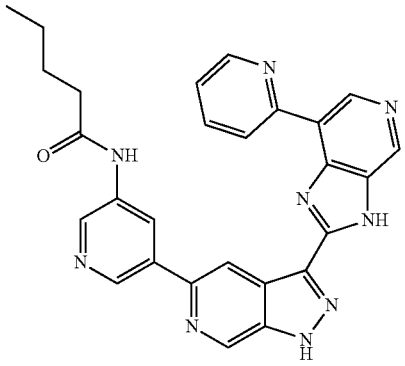
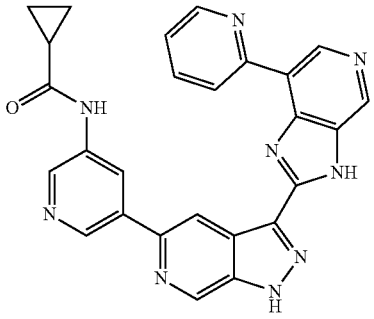
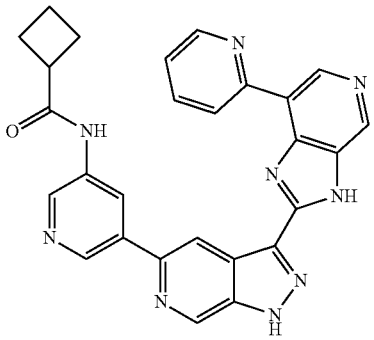
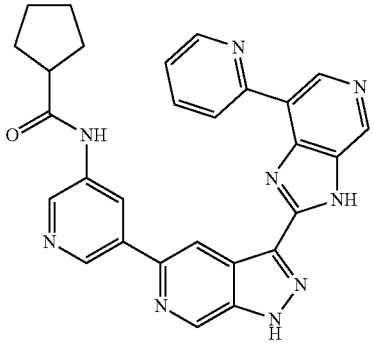
144	
145	
146	
147	

TABLE 1-continued

148	
149	
150	
151	

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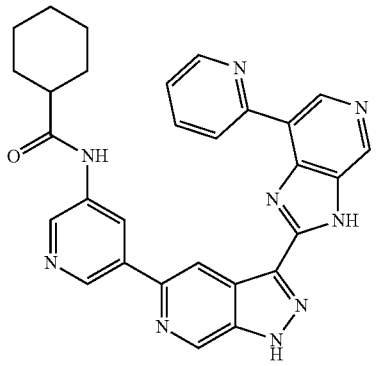
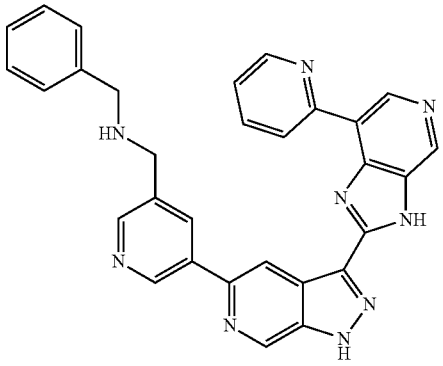
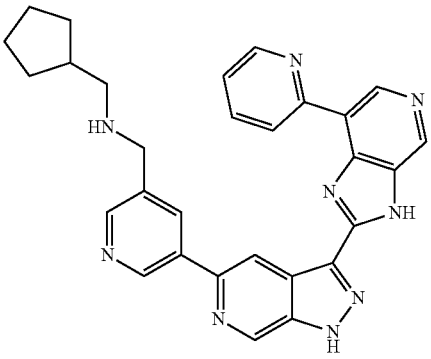
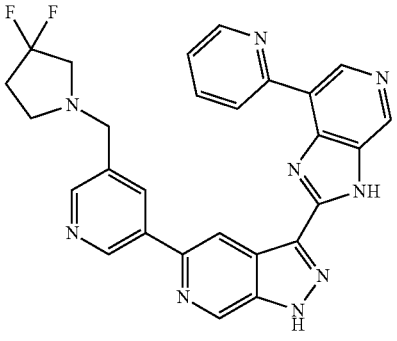
152	
153	
154	
155	

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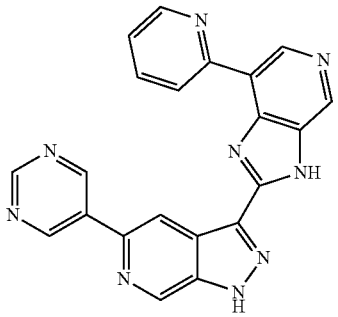
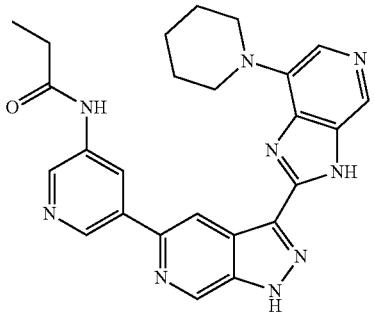
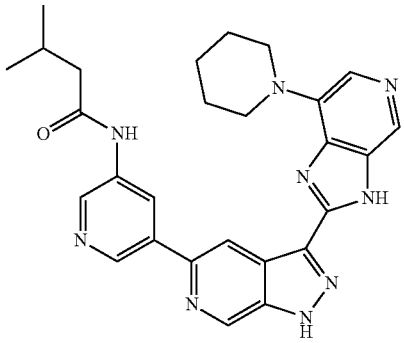
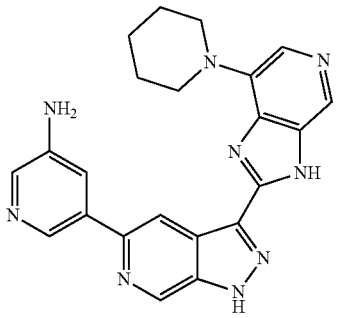
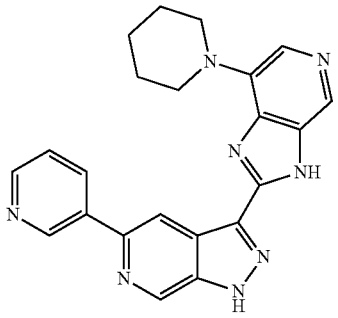
156	
157	
158	
159	
160	

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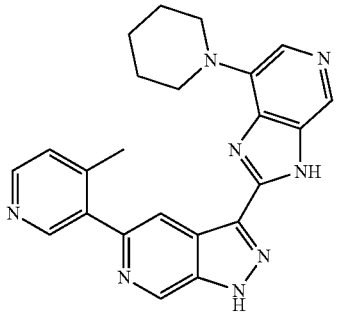
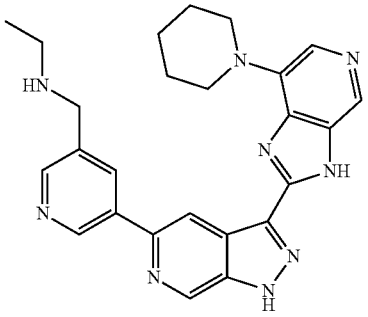
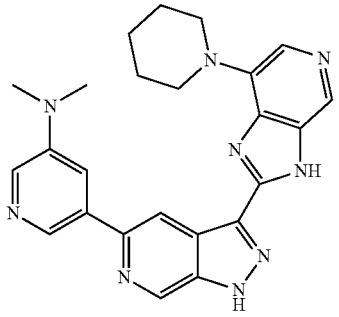
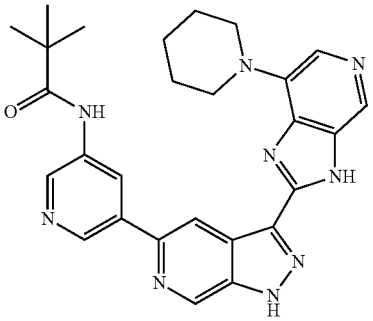
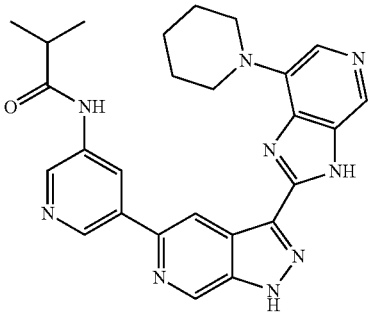
161	
162	
163	
164	
165	

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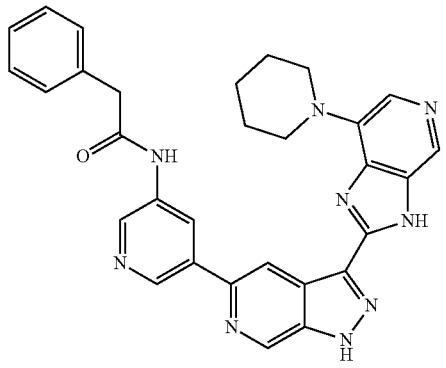

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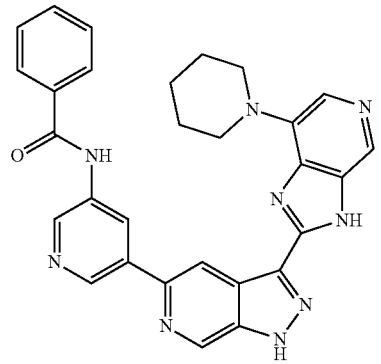

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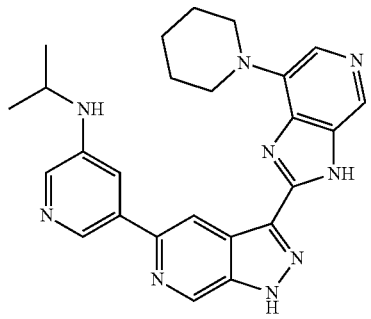

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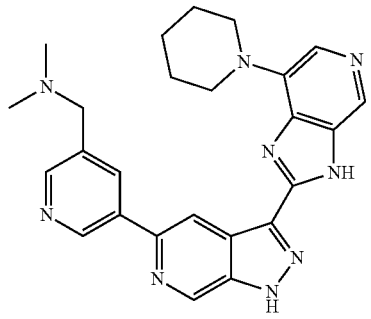

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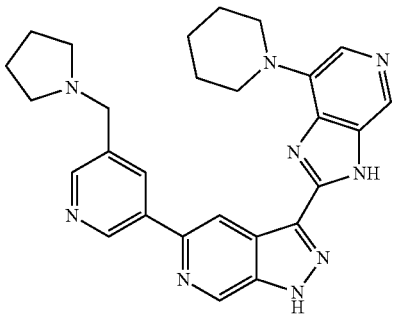

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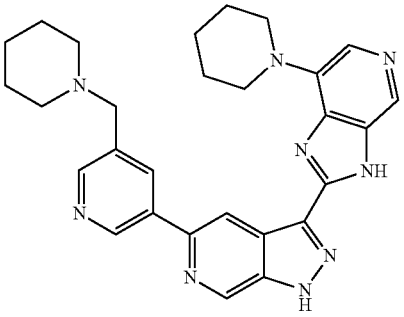

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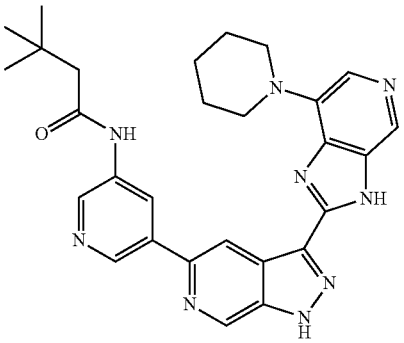

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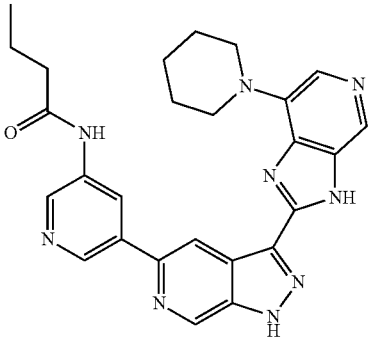

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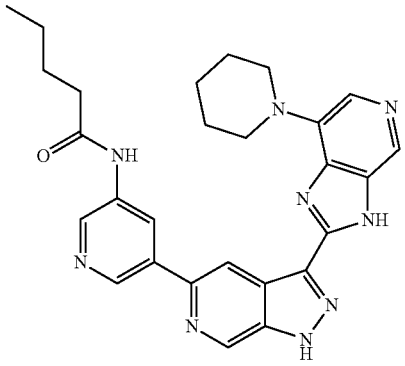
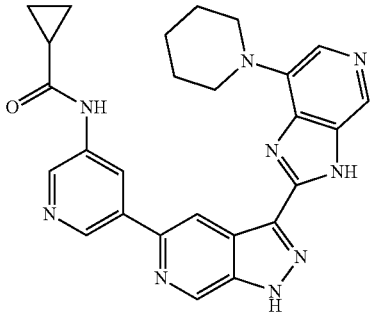
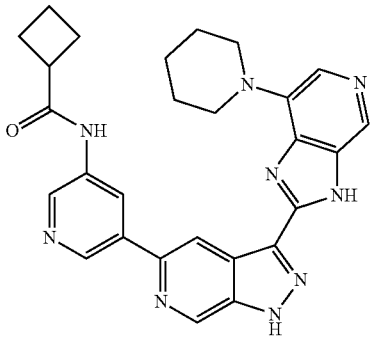
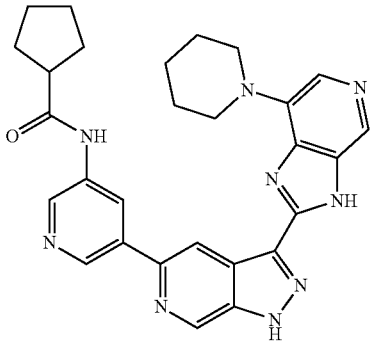
174	
175	
176	
177	

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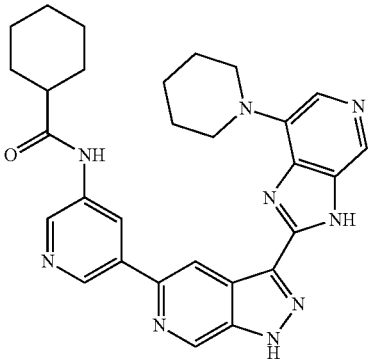
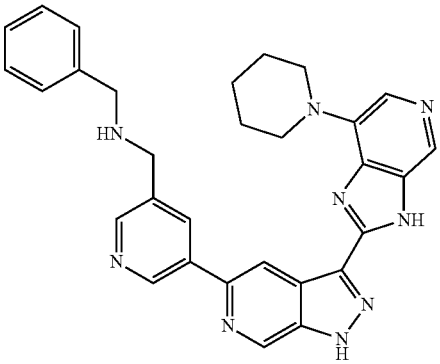
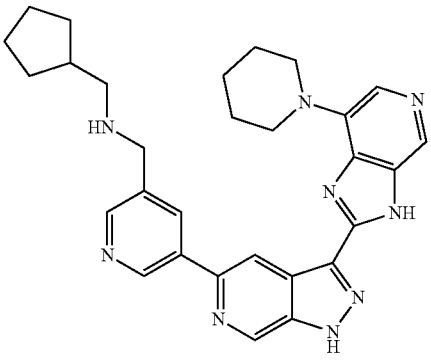
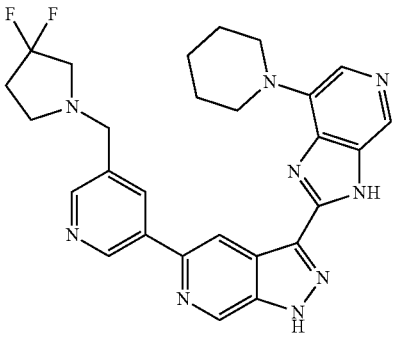
178	
179	
180	
181	

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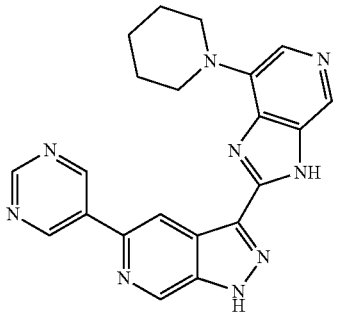
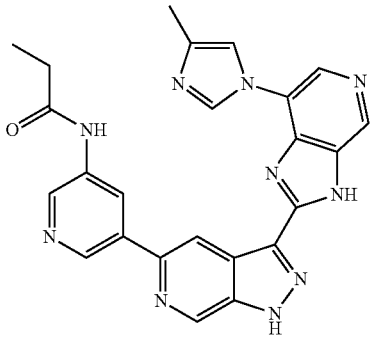
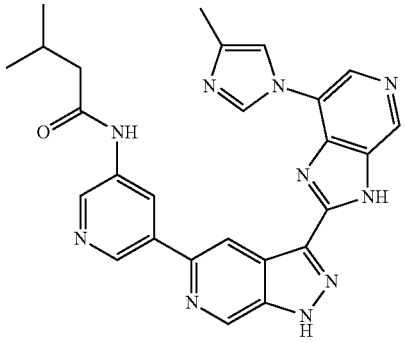
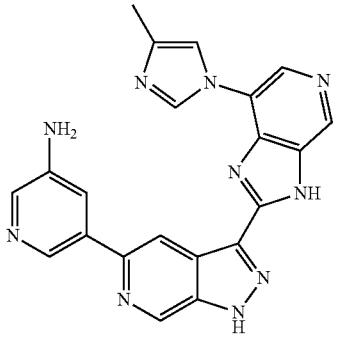
182	
183	
184	
185	

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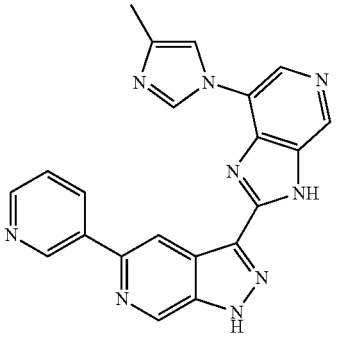
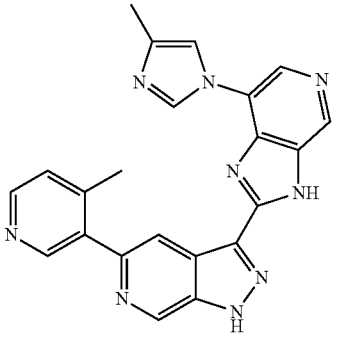
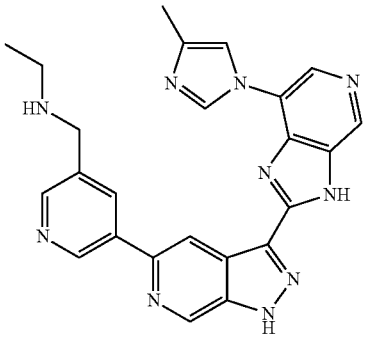
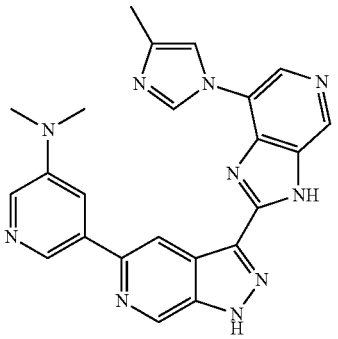
186	
187	
188	
189	

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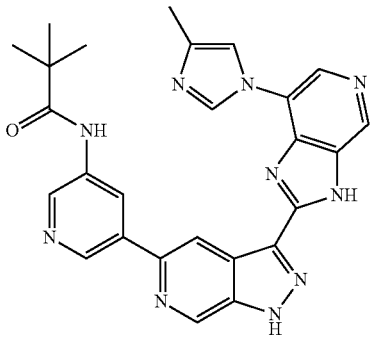
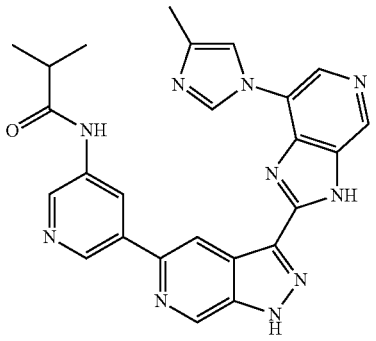
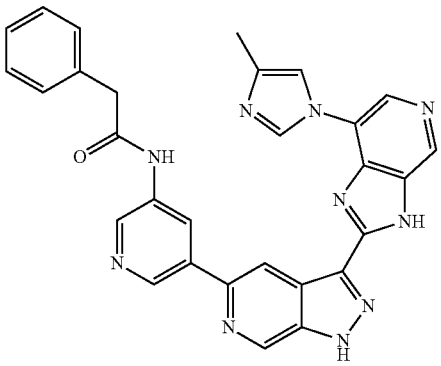
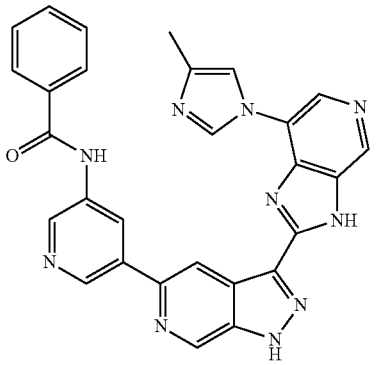
190	
191	
192	
193	

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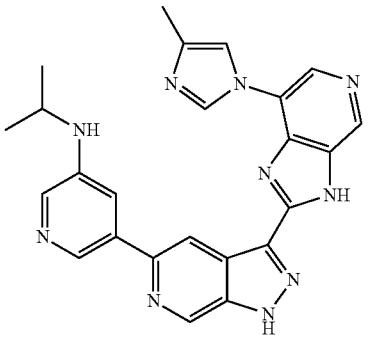
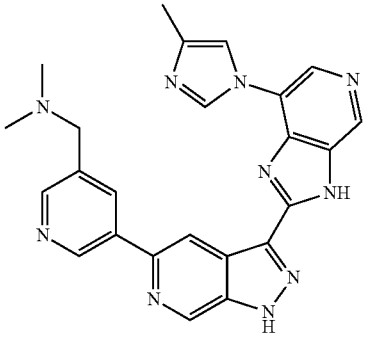
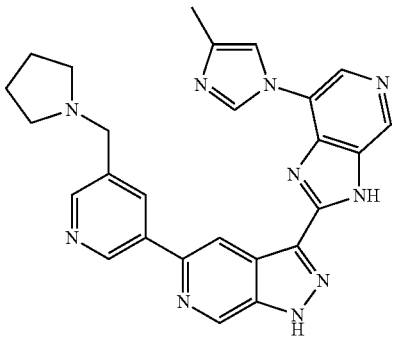
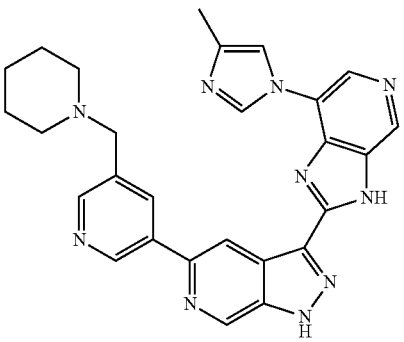
194	
195	
196	
197	

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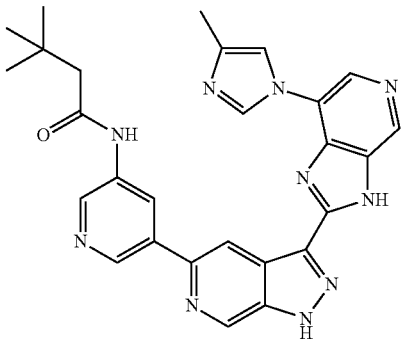
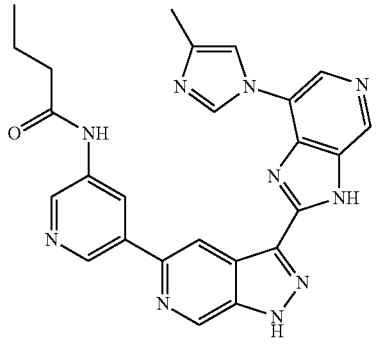
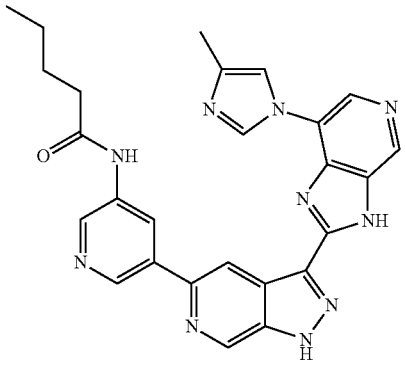
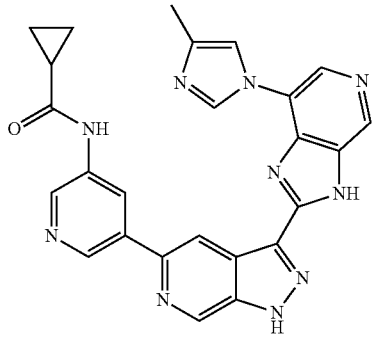
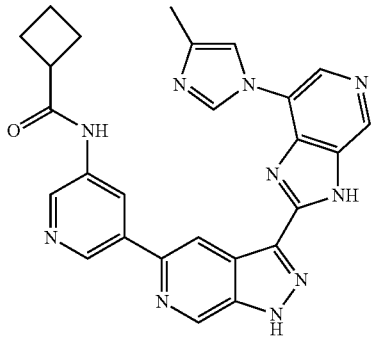
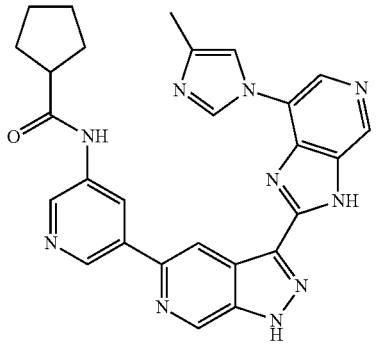
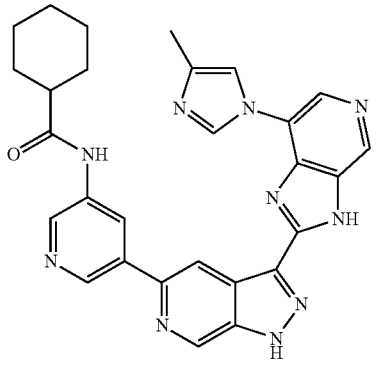
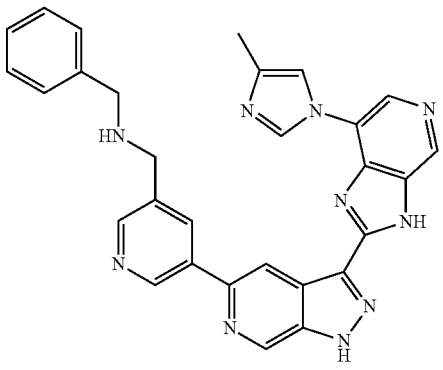
198	
199	
200	
201	

TABLE 1-continued

202	
203	
204	
205	

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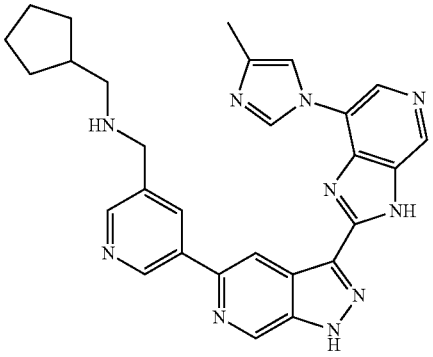
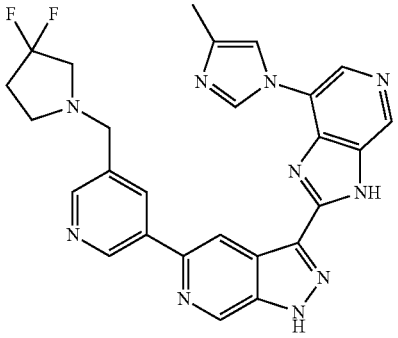
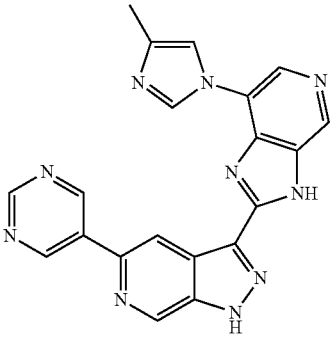
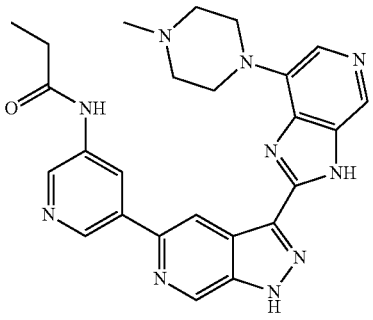
206	
207	
208	
209	

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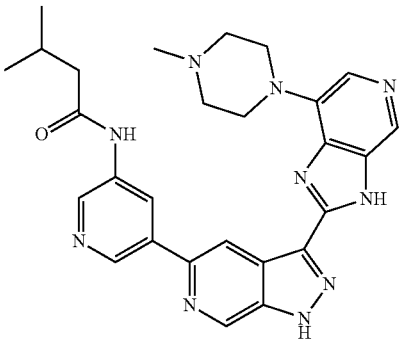
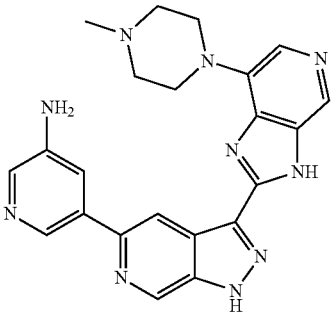
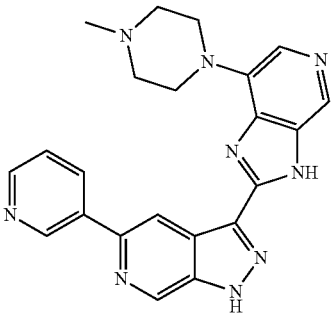
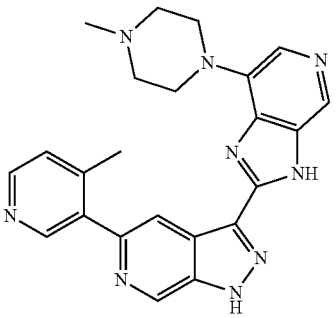
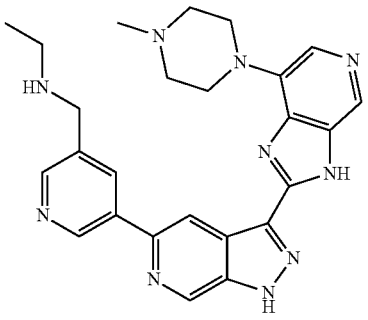
210	
211	
212	
213	
214	

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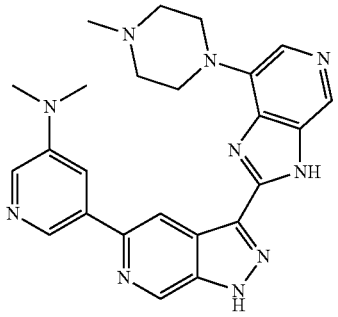
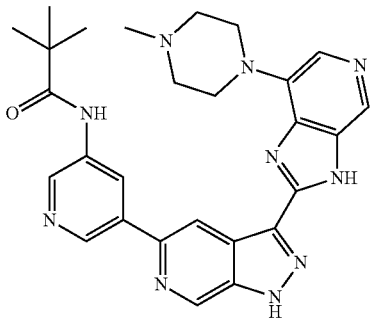
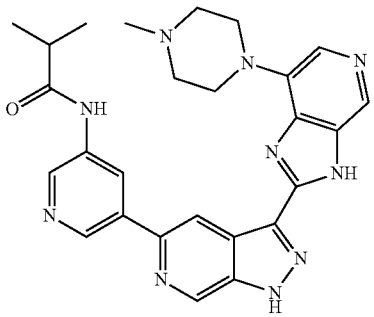
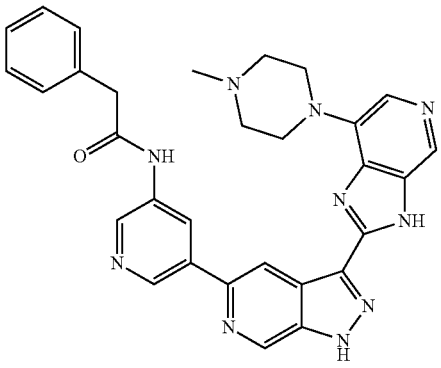
215	
216	
217	
218	

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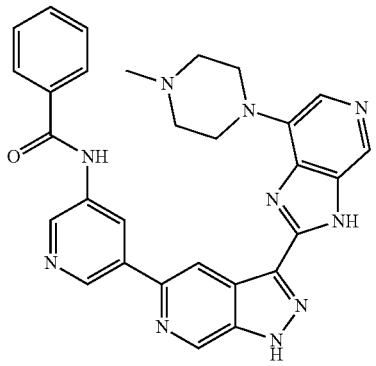
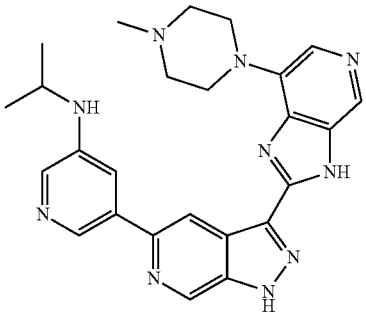
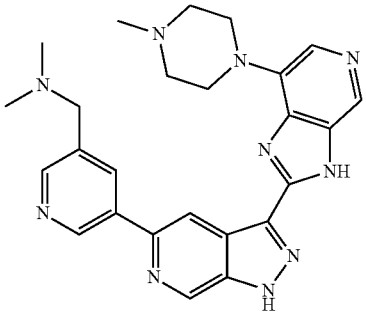
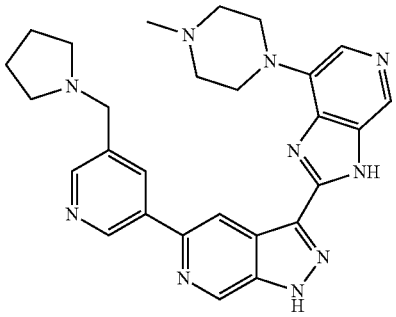
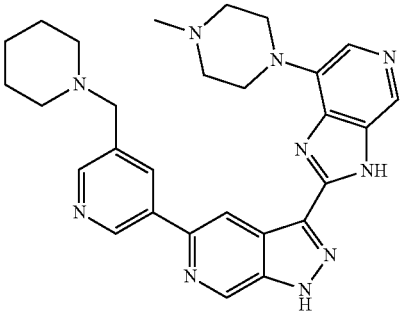
219	
220	
221	
222	
223	

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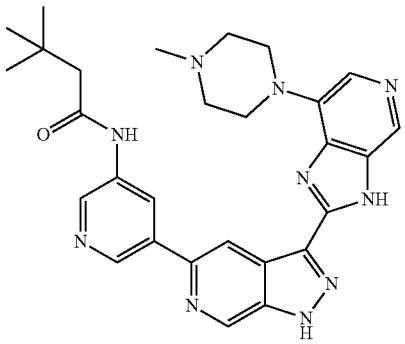
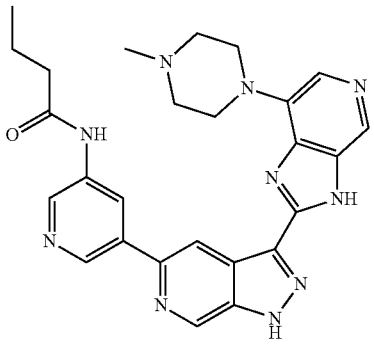
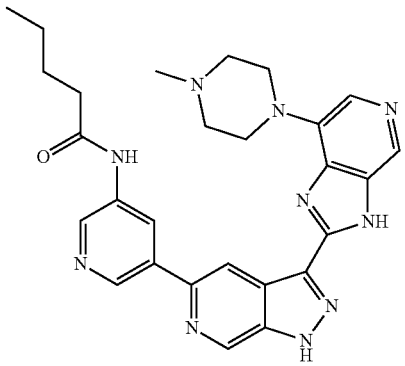
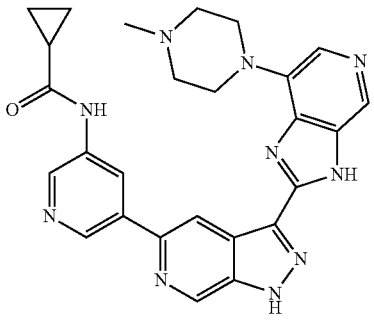
224	
225	
226	
227	

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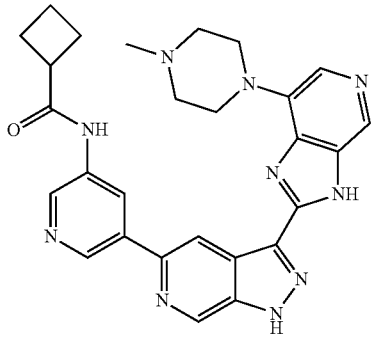
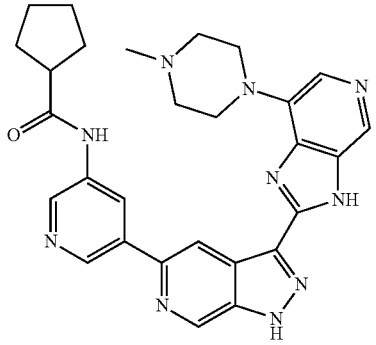
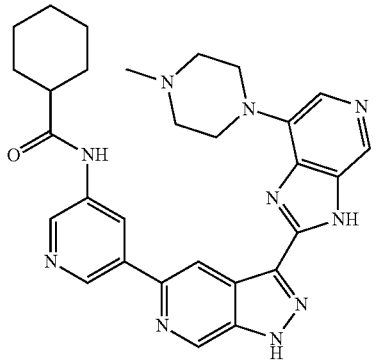
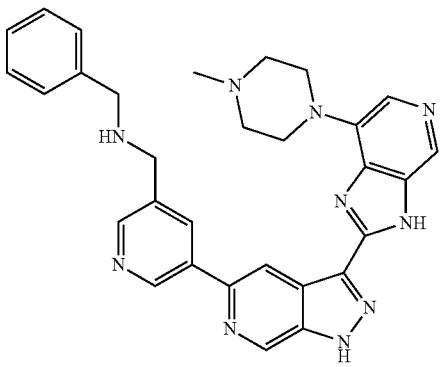
228	
229	
230	
231	

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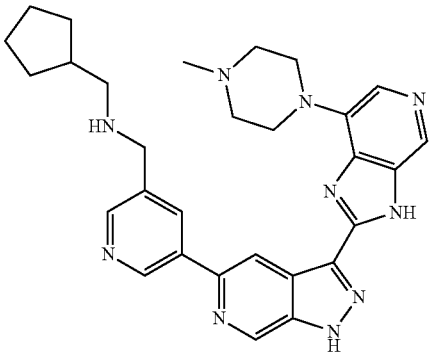
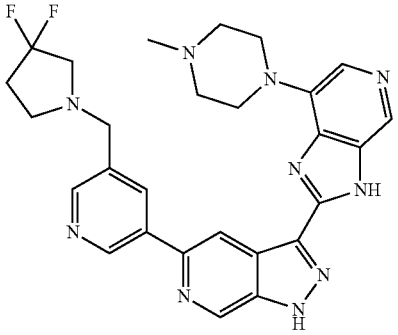
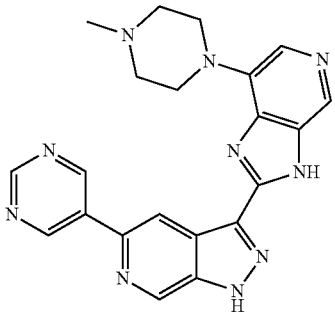
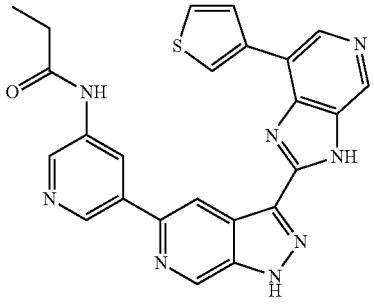
232	
233	
234	
235	

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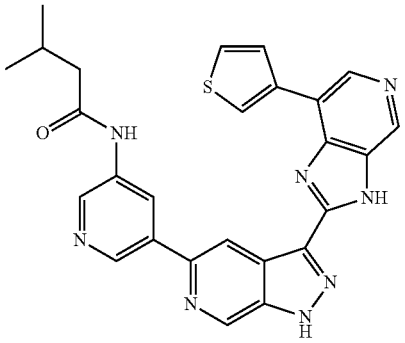
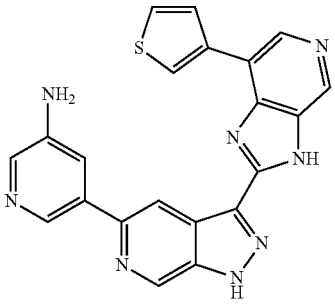
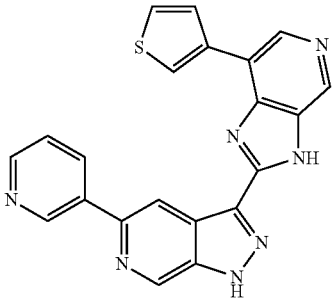
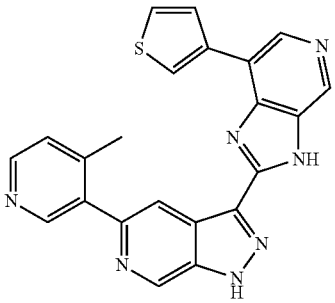
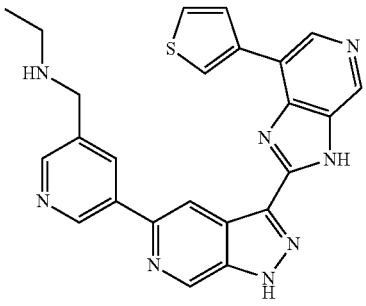
236	
237	
238	
239	
240	

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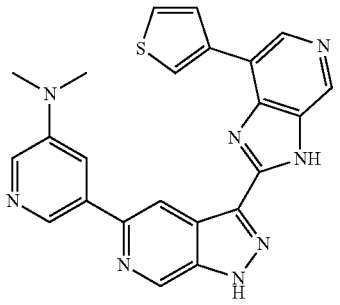
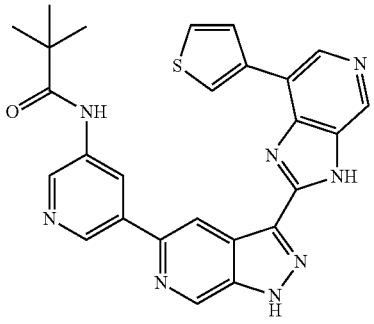
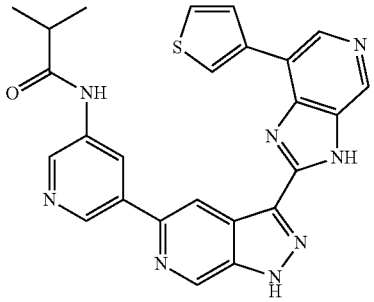
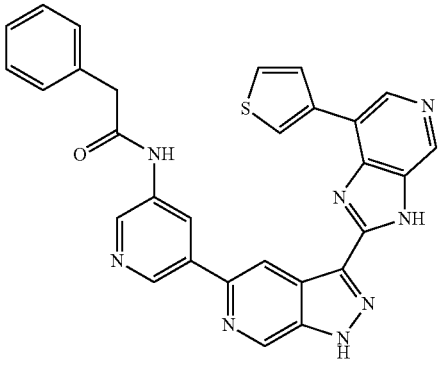
241	
242	
243	
244	

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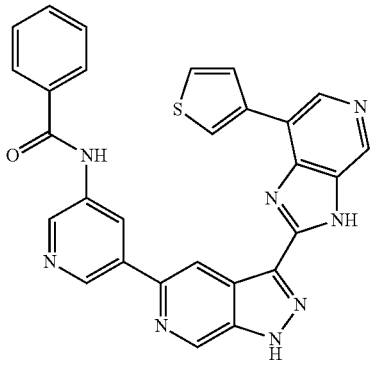
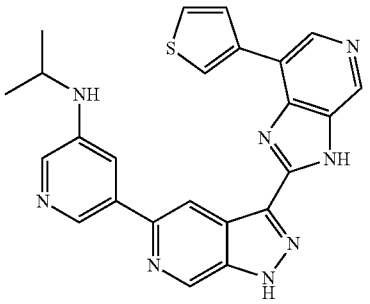
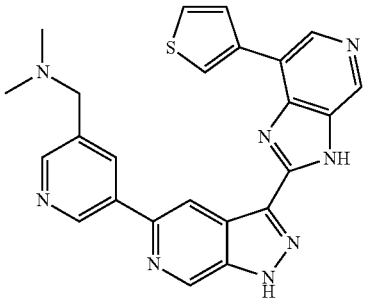
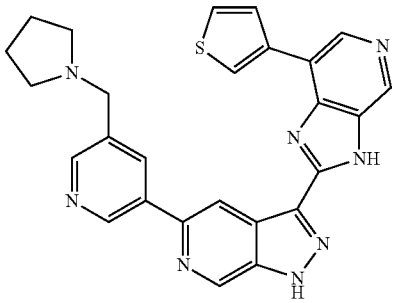
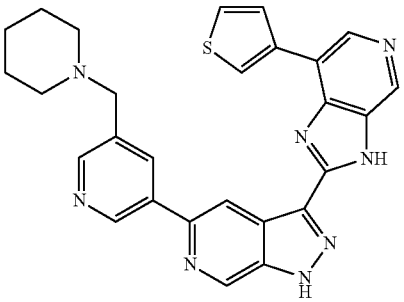
245	
246	
247	
248	
249	

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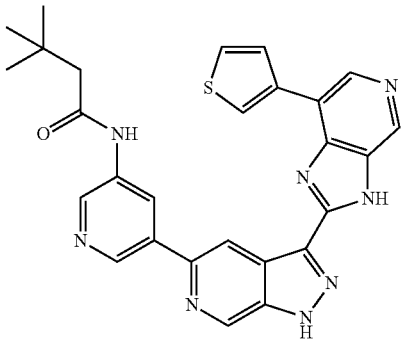
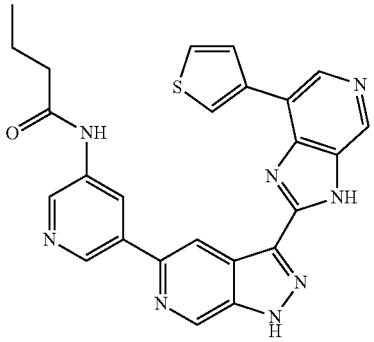
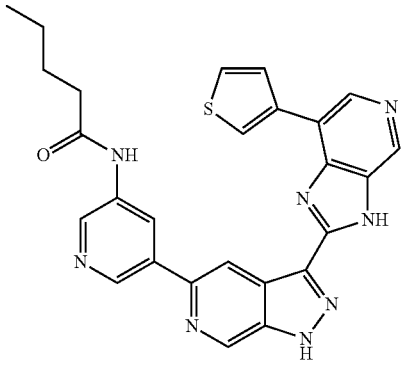
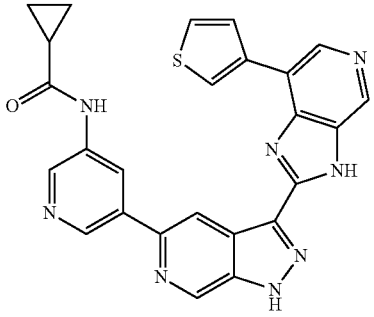
250	
251	
252	
253	

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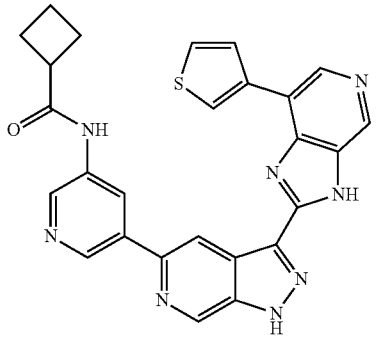
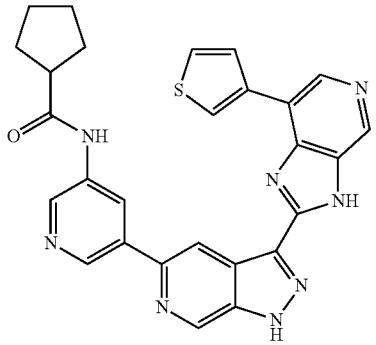
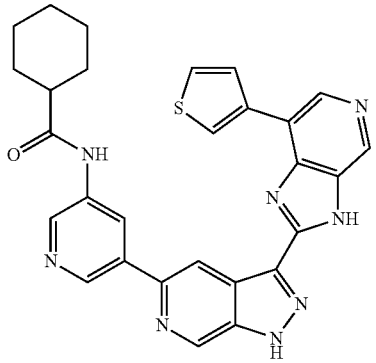
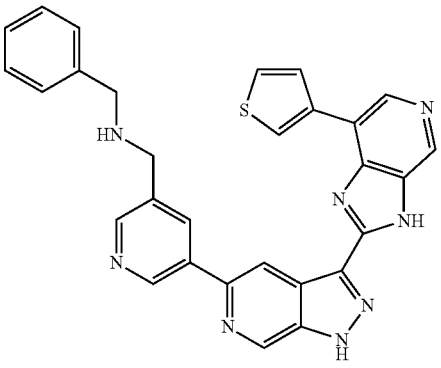
254	
255	
256	
257	

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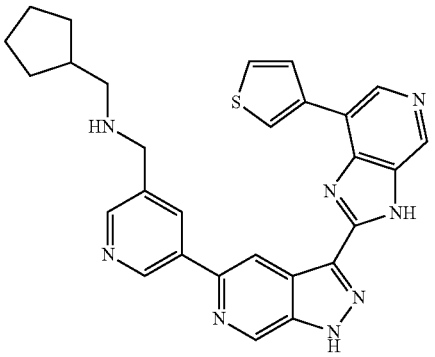
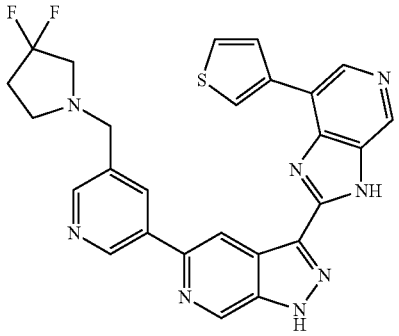
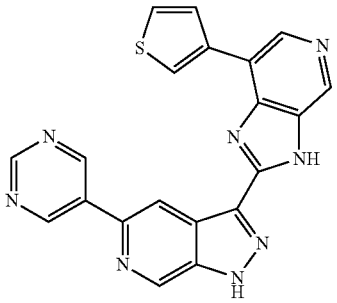
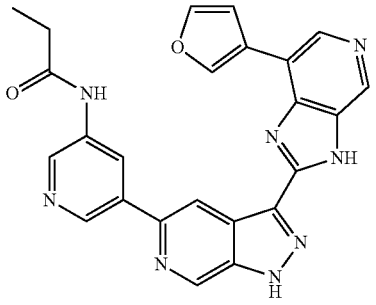
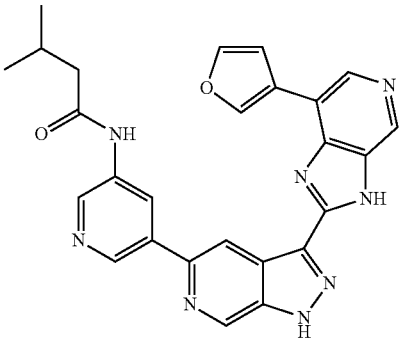
258	
259	
260	
261	
262	

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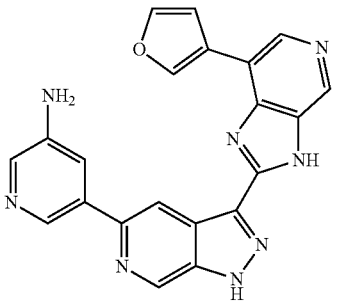
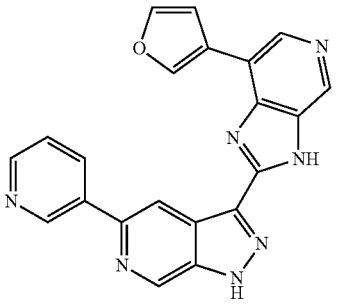
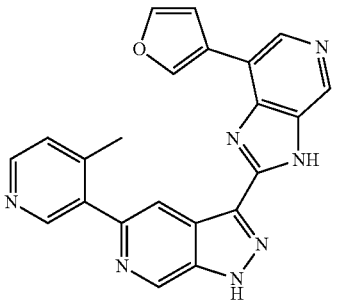
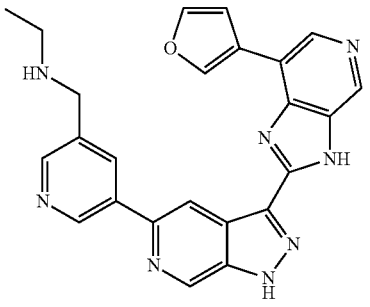
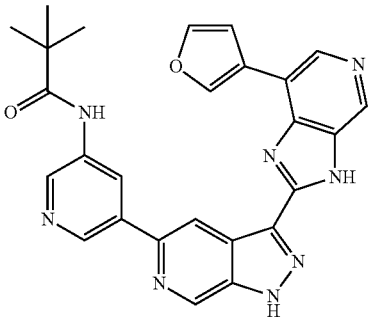
263	
264	
265	
266	
267	

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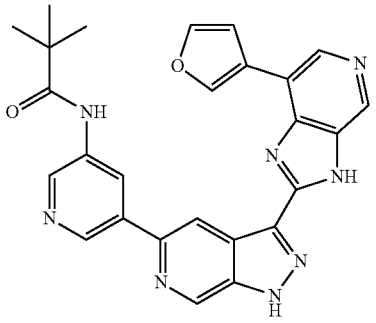
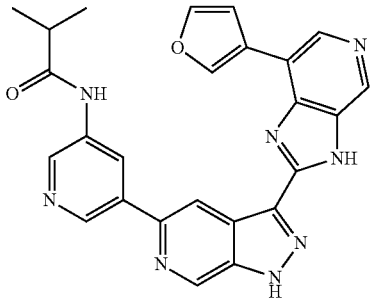
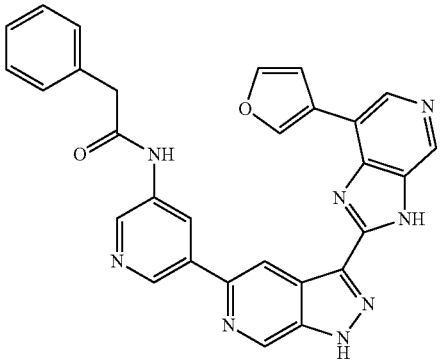
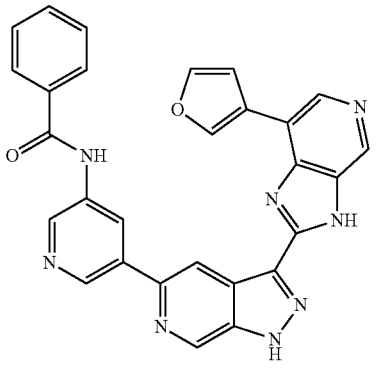
268	
269	
270	
271	

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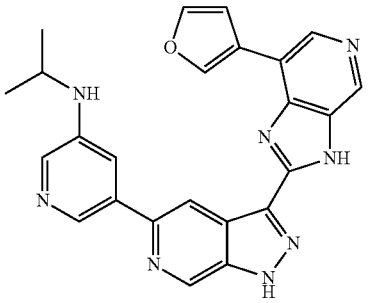
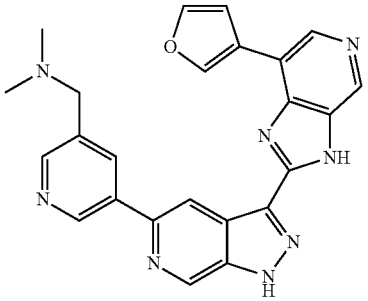
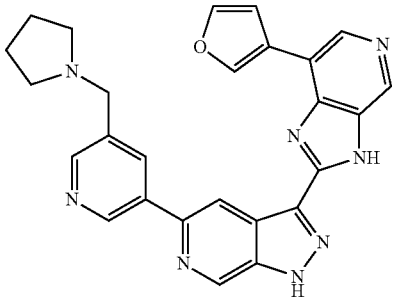
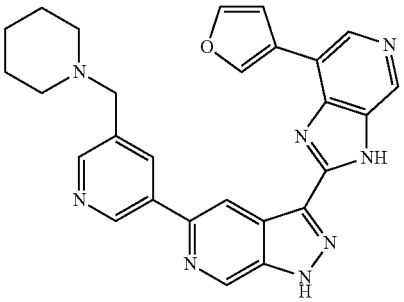
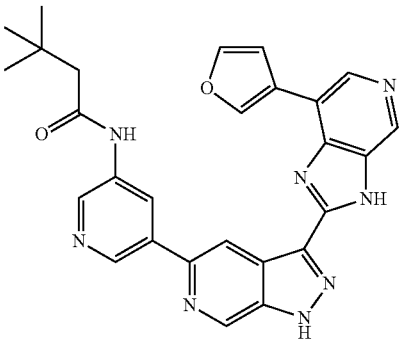
272	
273	
274	
275	
276	

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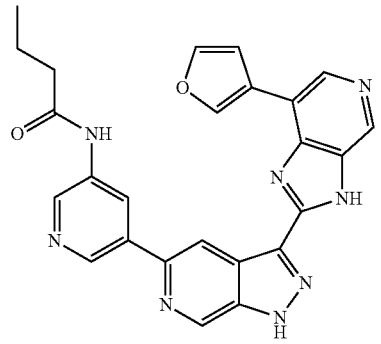
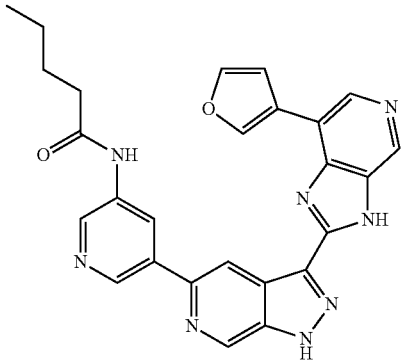
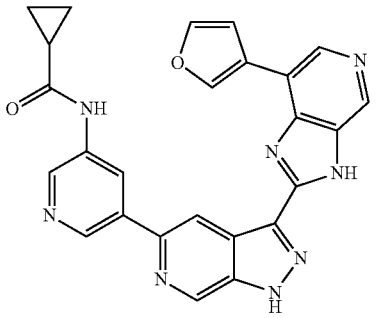
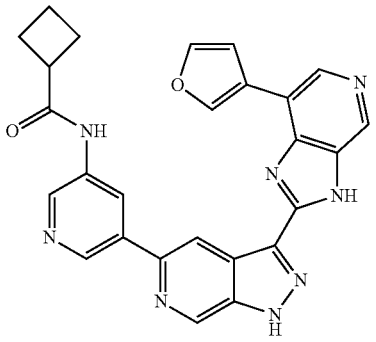
277	
278	
279	
280	

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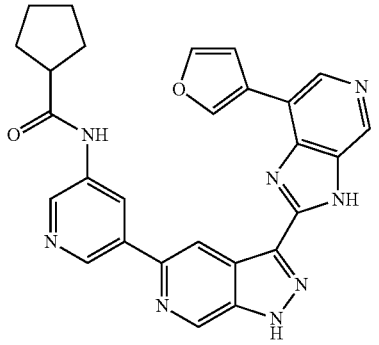
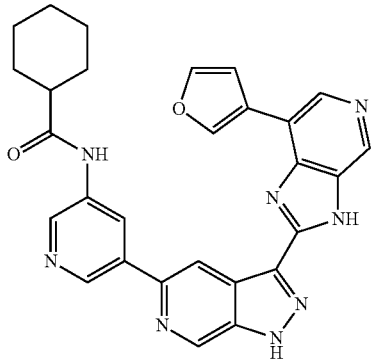
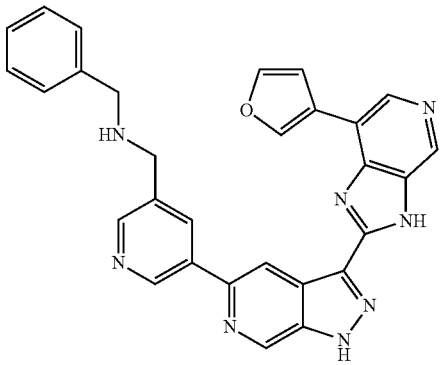
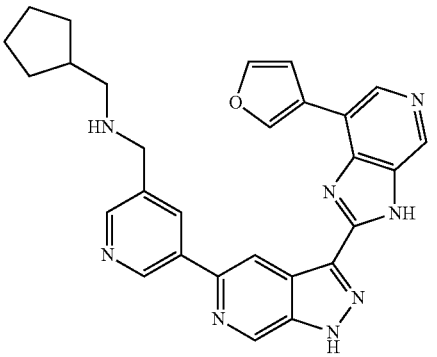
281	
282	
283	
284	

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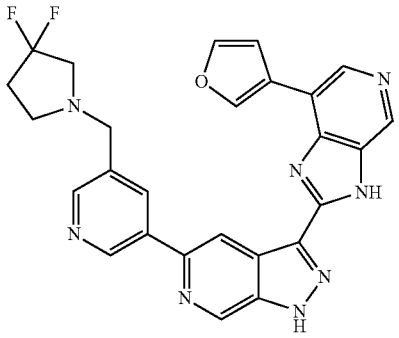
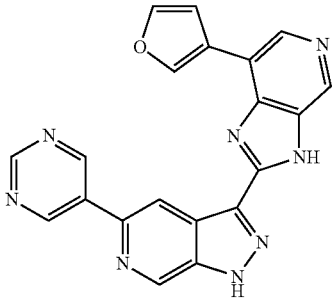
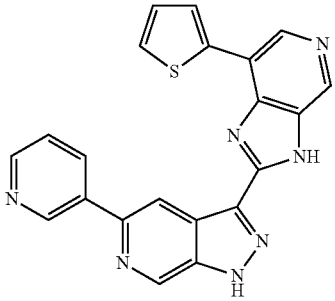
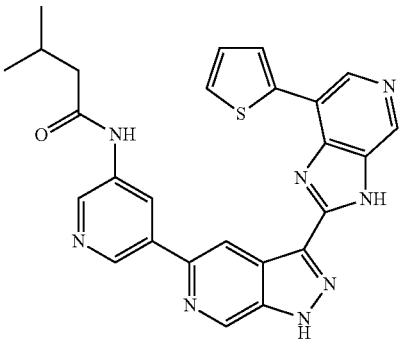
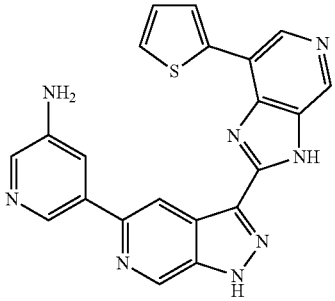
285	
286	
287	
288	
289	

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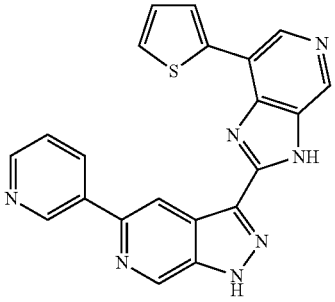
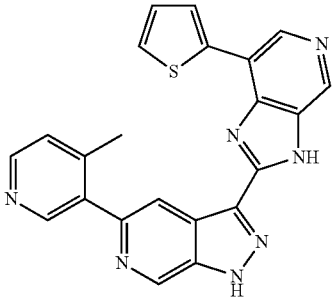
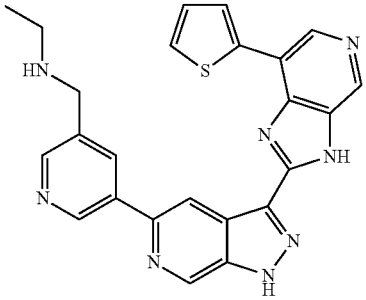
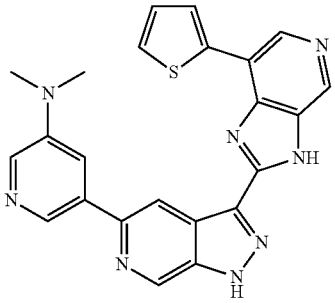
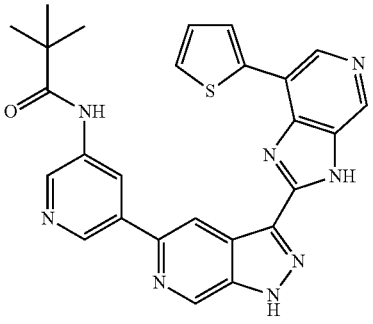
290	
291	
292	
293	
294	

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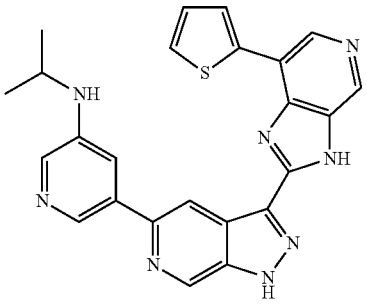
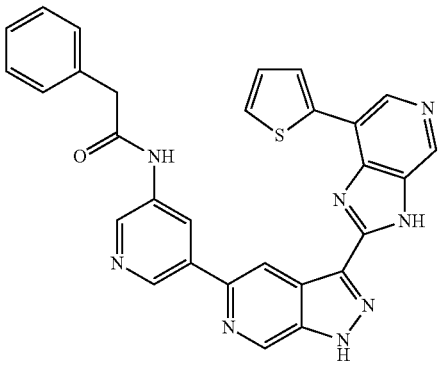
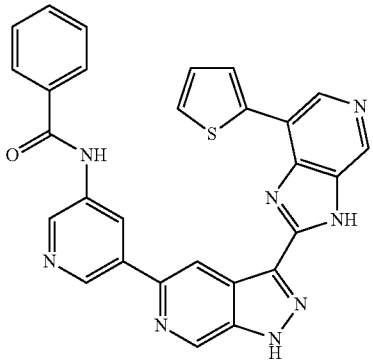
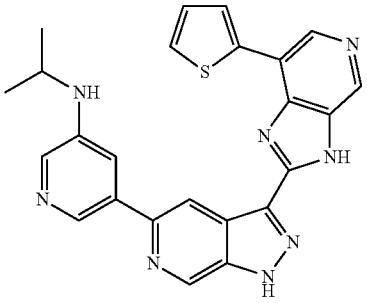
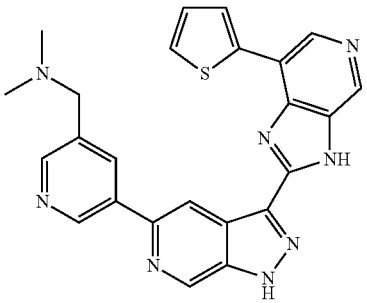
295	
296	
297	
298	
299	

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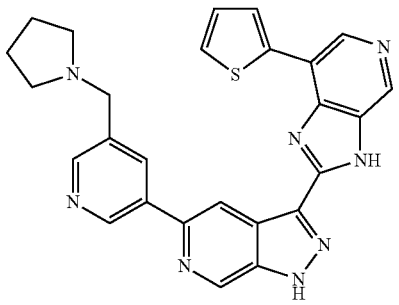
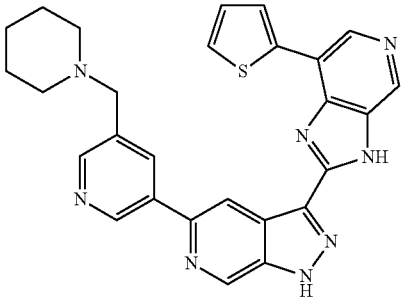
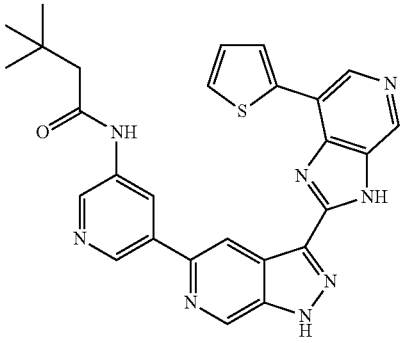
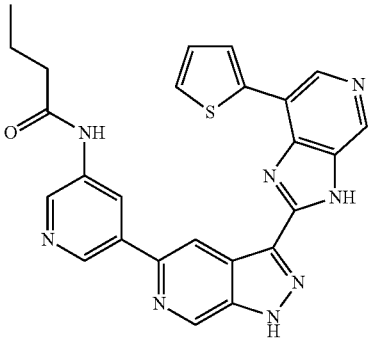
300	
301	
302	
303	

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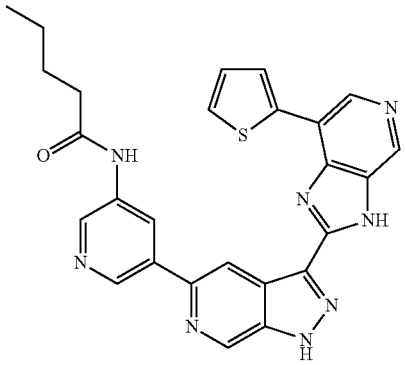
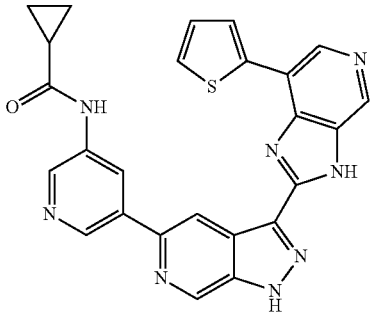
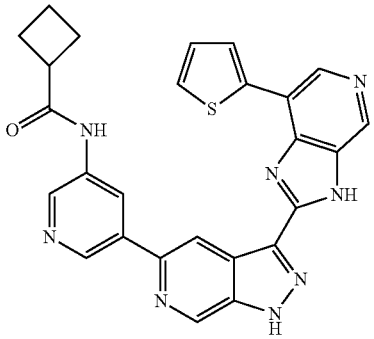
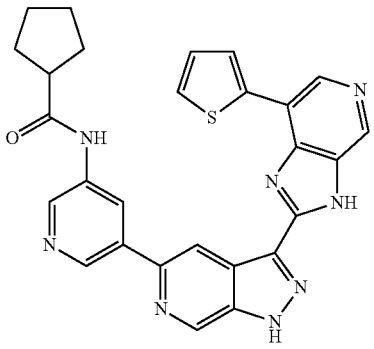
304	
305	
306	
307	

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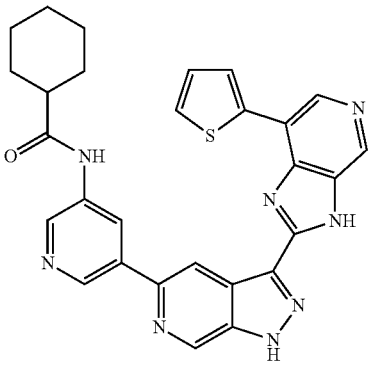
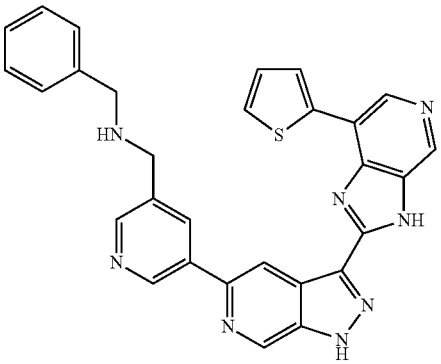
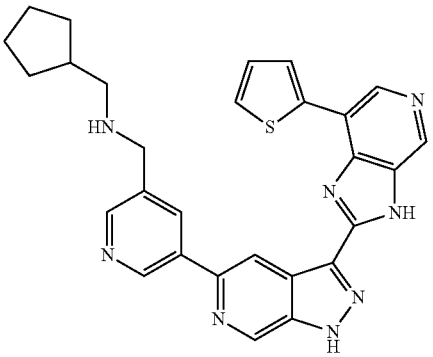
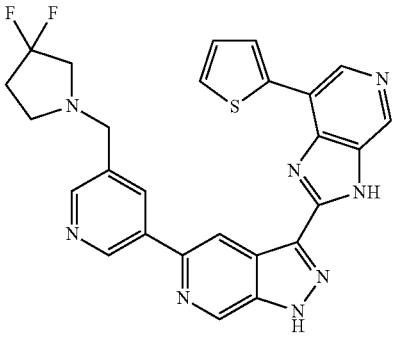
308	
309	
310	
311	

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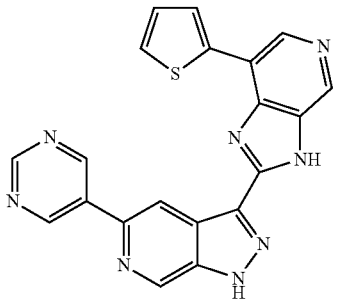
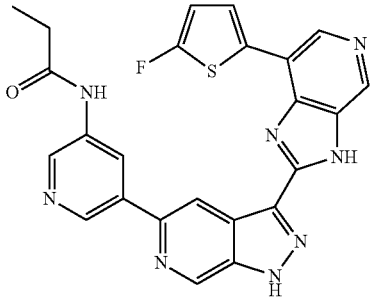
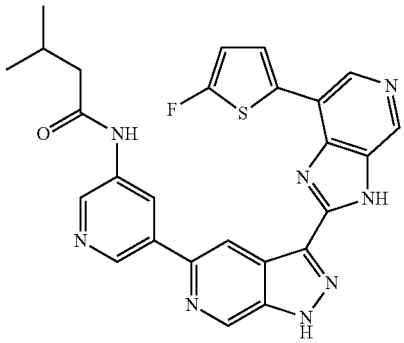
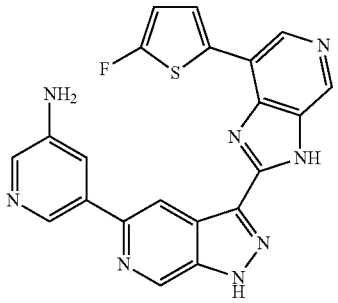
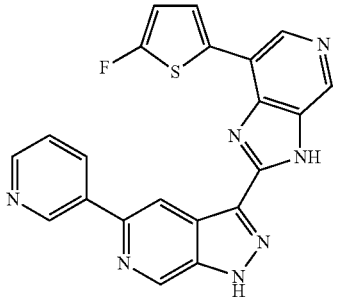
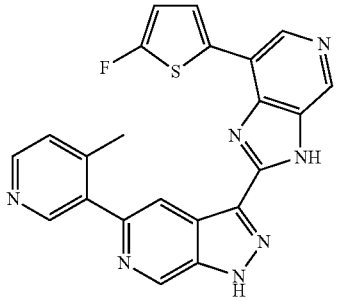
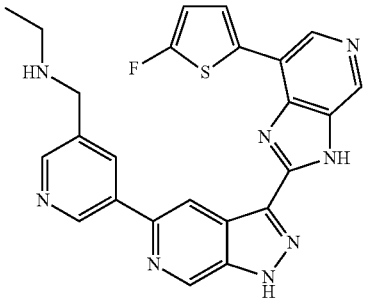
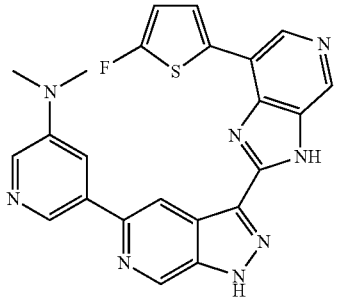
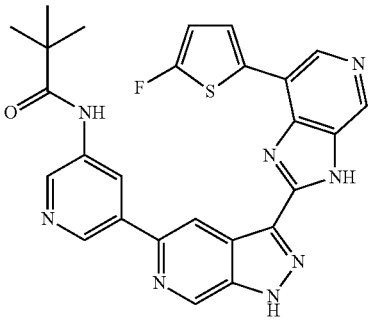
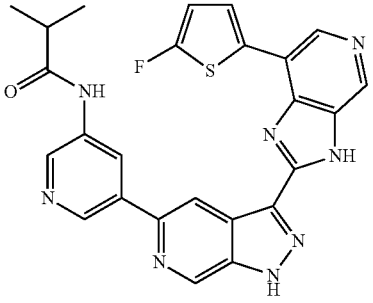
312	
313	
314	
315	
316	

TABLE 1-continued

317	
318	
319	
320	
321	

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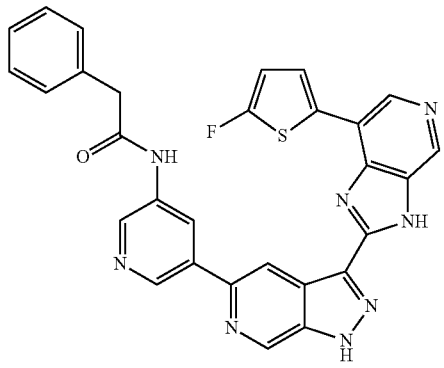
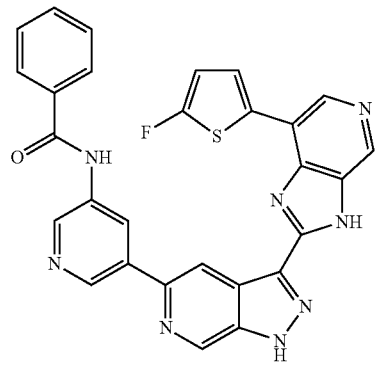
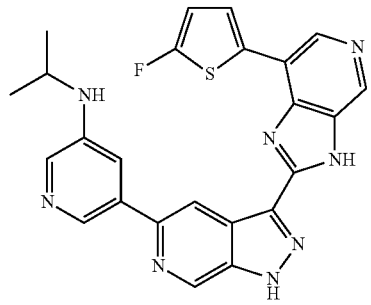
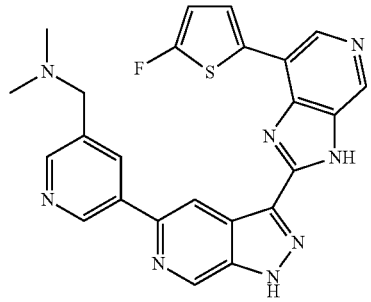
322	
323	
324	
325	

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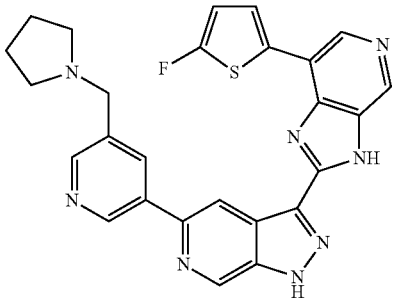
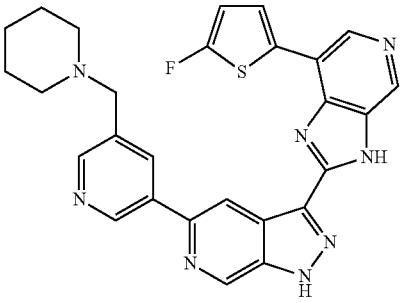
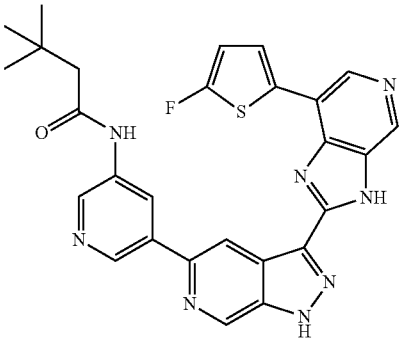
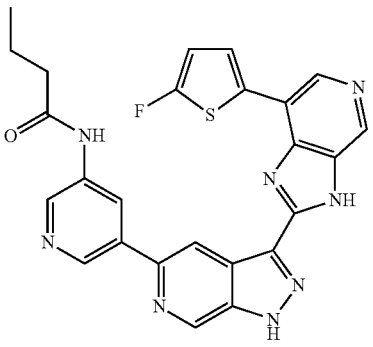
326	
327	
328	
329	

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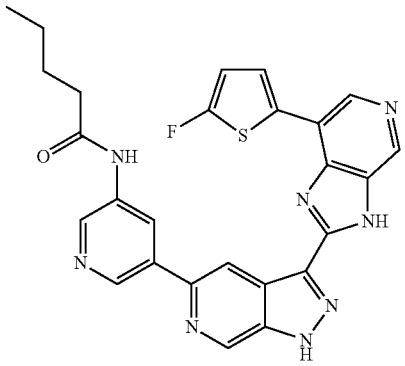
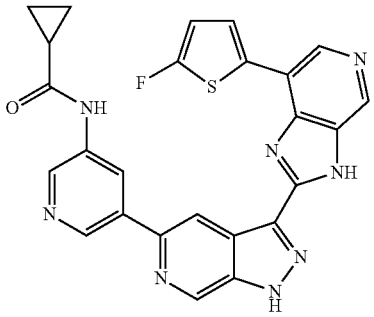
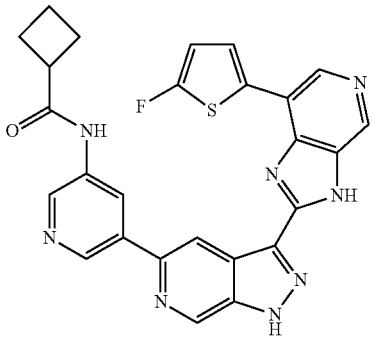
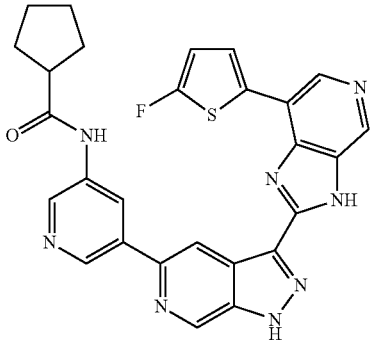
330	
331	
332	
333	

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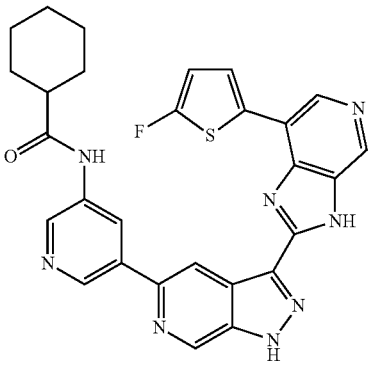
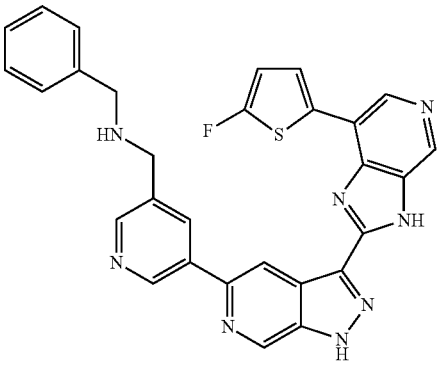
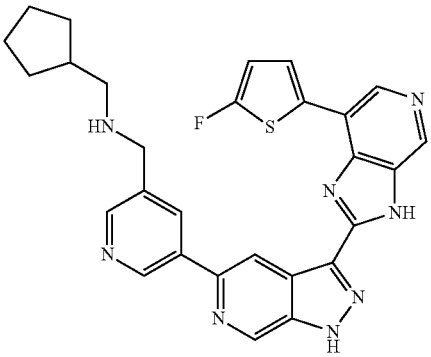
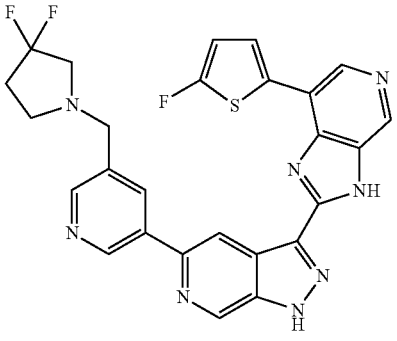
334	
335	
336	
337	

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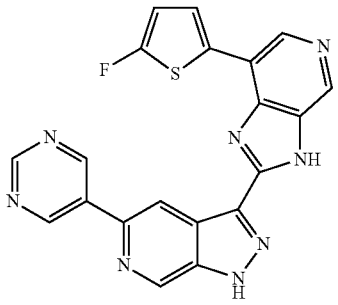
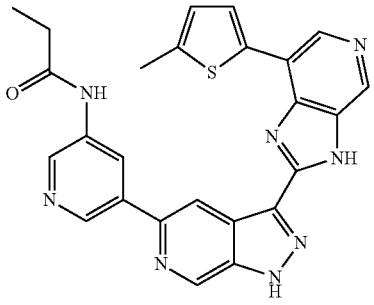
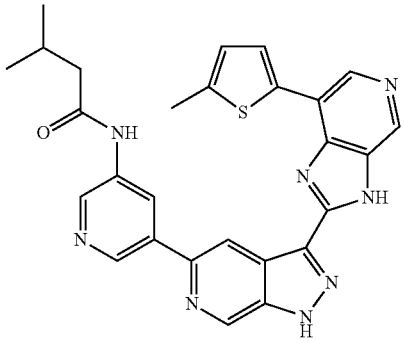
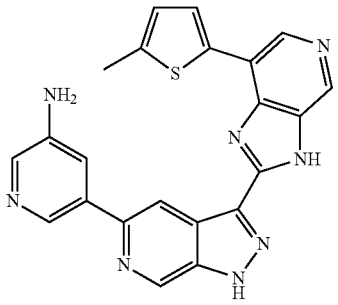
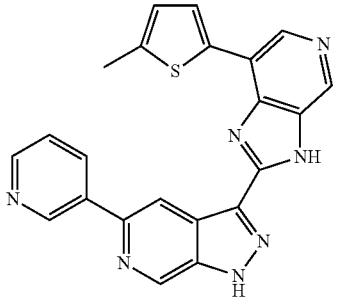
338	
339	
340	
341	
342	

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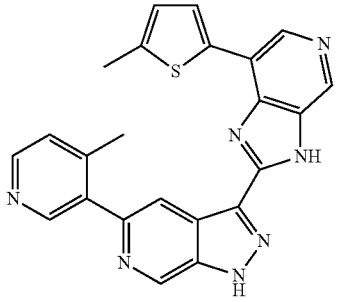
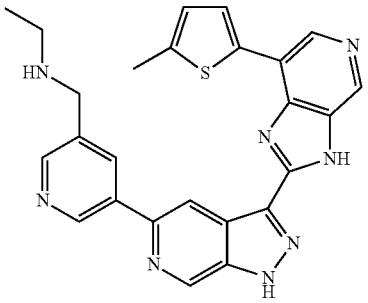
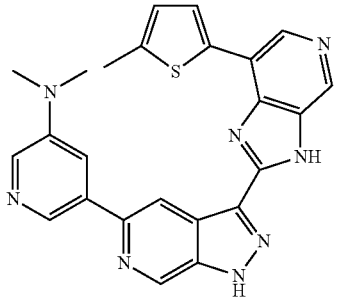
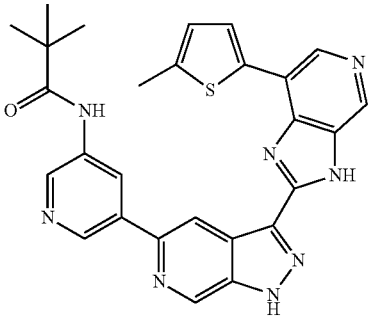
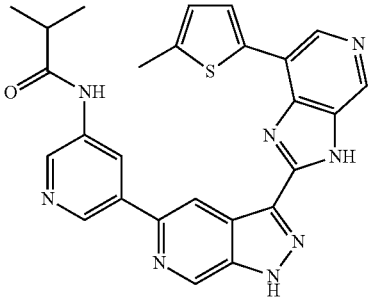
343	
344	
345	
346	
347	

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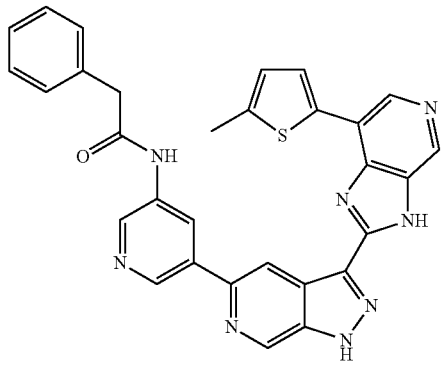
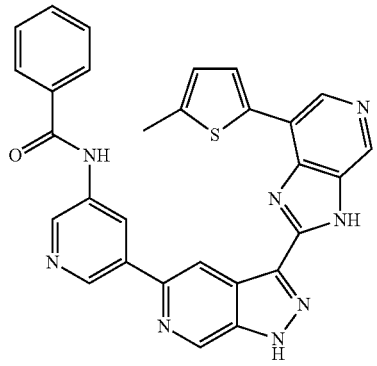
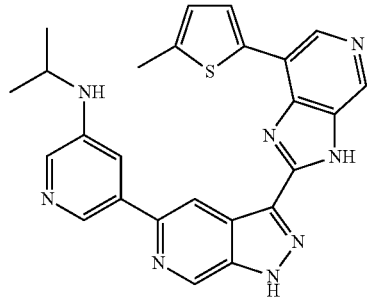
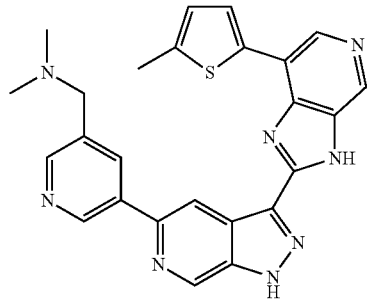
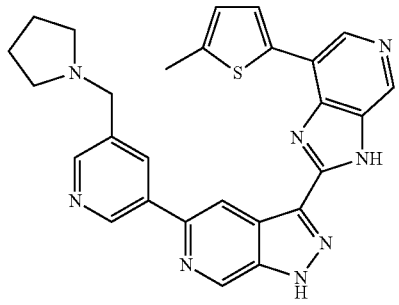
348	
349	
350	
351	
352	

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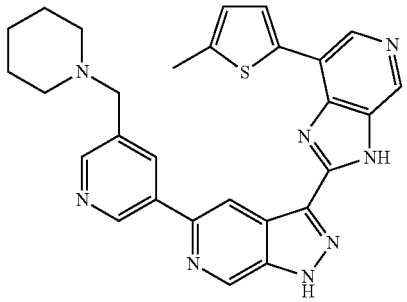
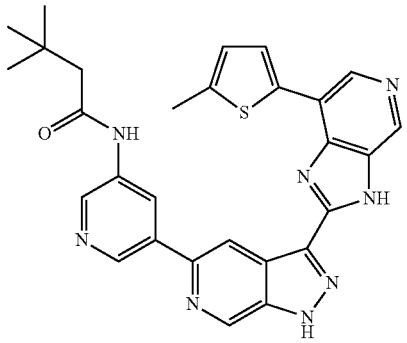
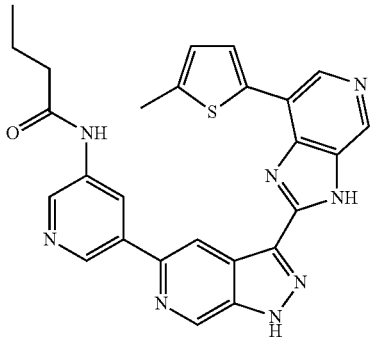
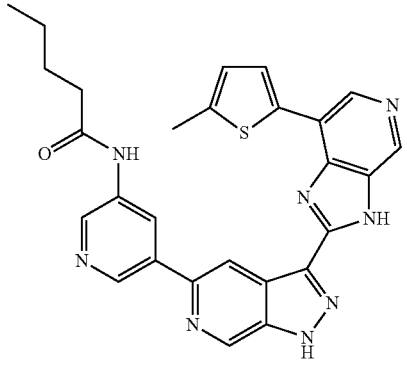
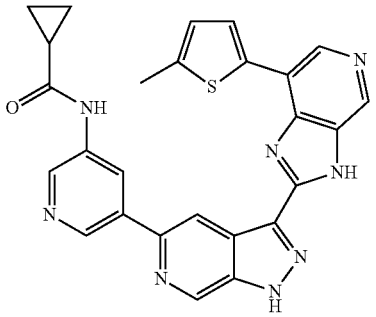
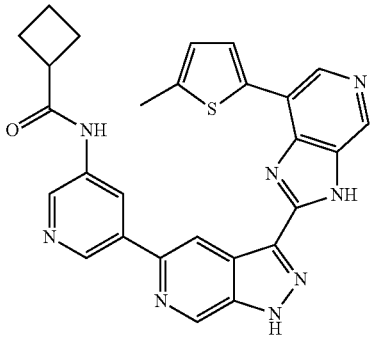
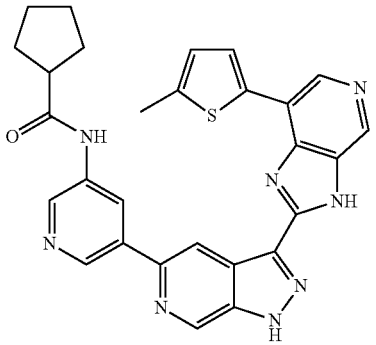
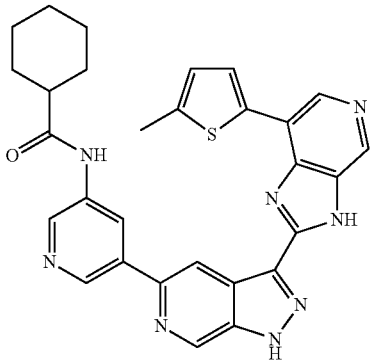
353	
354	
355	
356	

TABLE 1-continued

357	
358	
359	
360	

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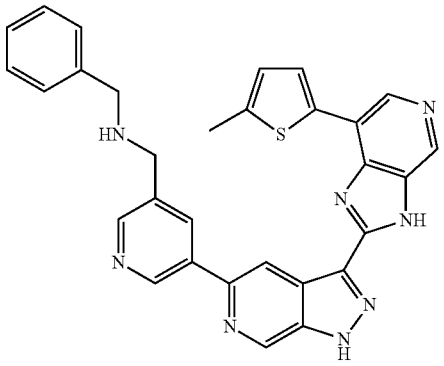
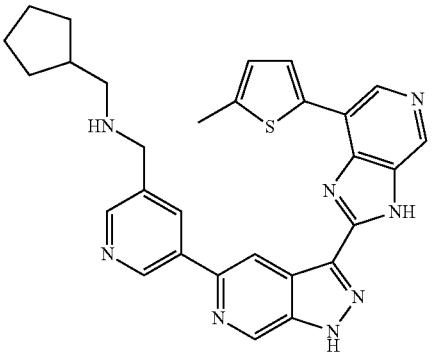
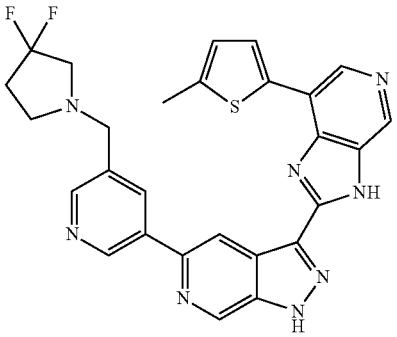
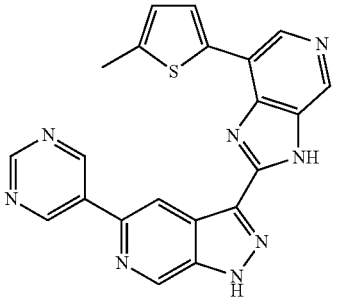
361	
362	
363	
364	

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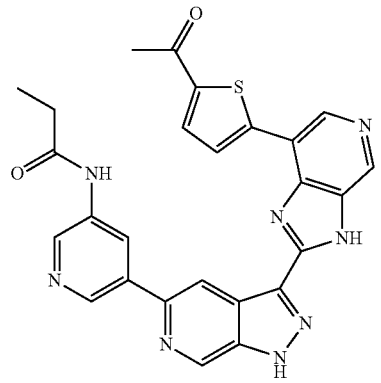
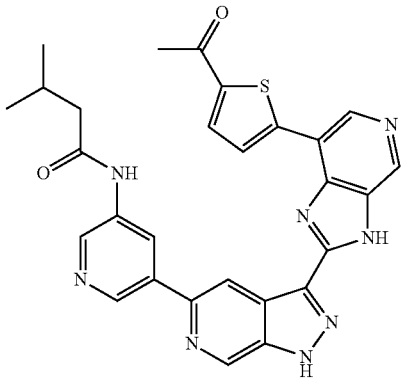
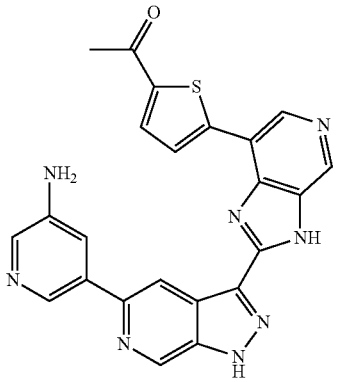
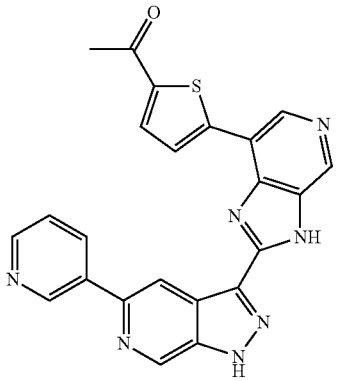
365	
366	
367	
368	

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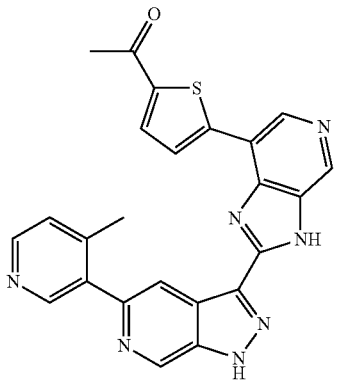
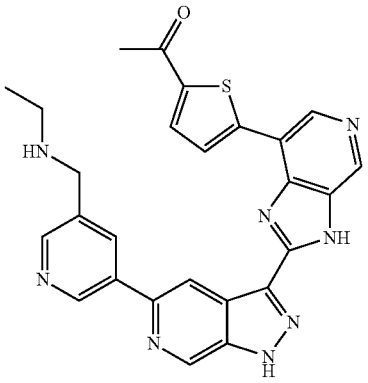
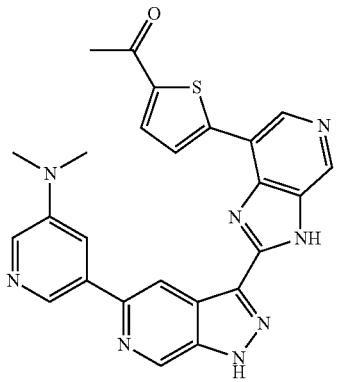
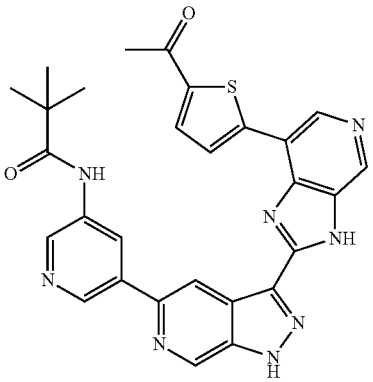
369	
370	
371	
372	

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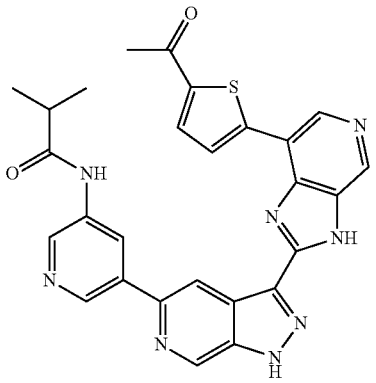
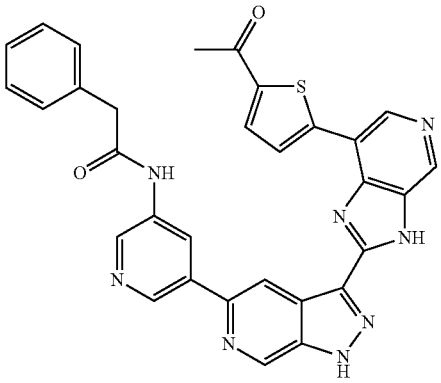
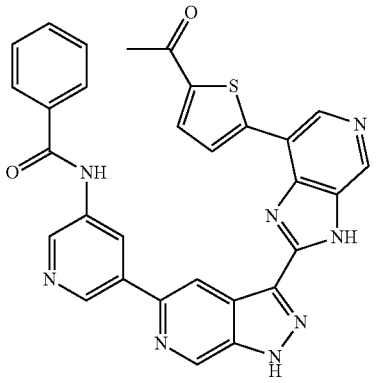
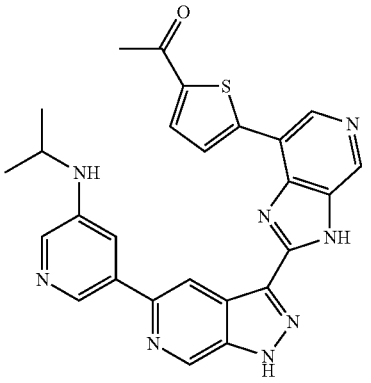
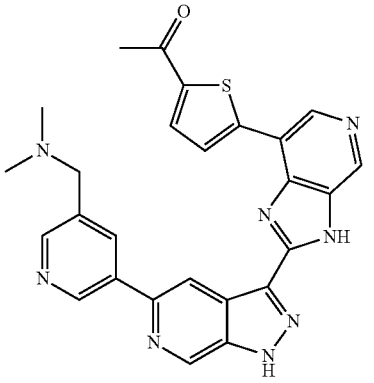
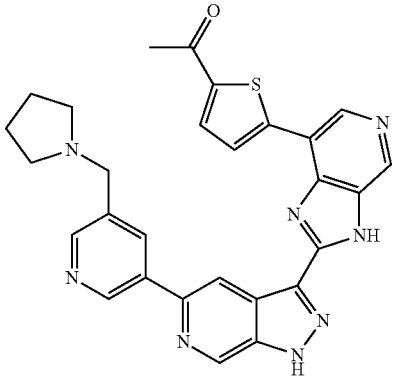
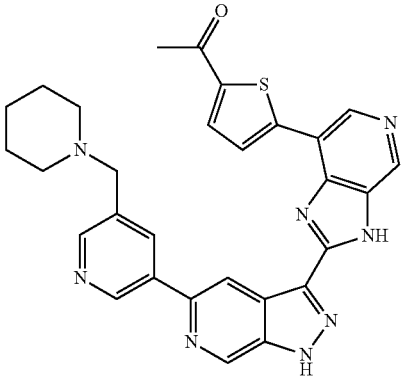
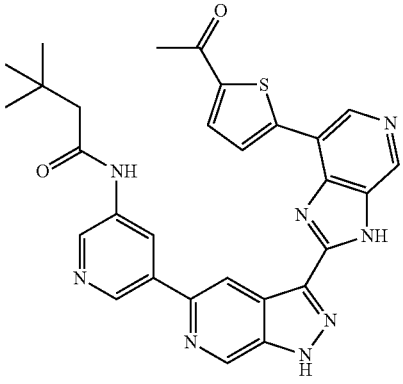
373	
374	
375	
376	

TABLE 1-continued

377	
378	
379	
380	

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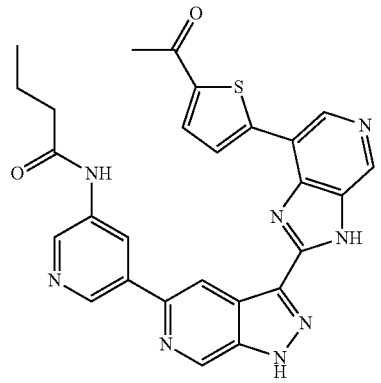
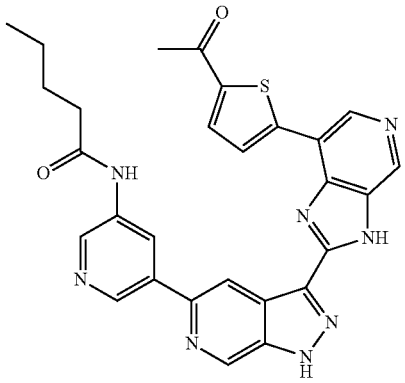
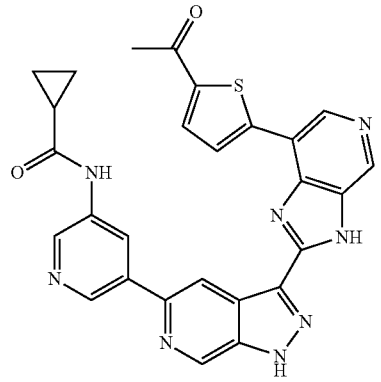
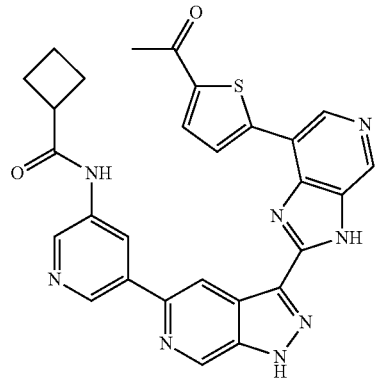
381	
382	
383	
384	

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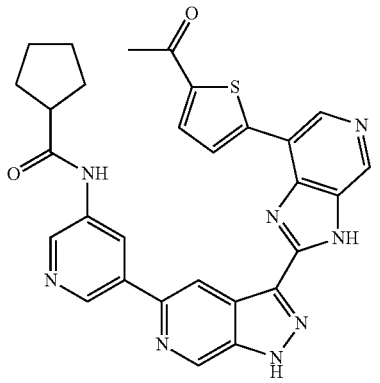
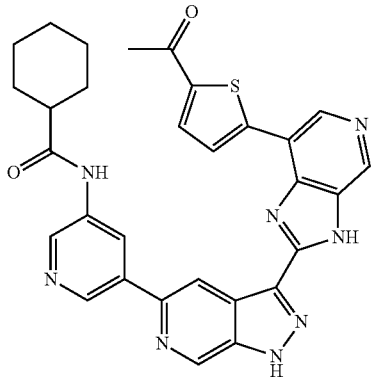
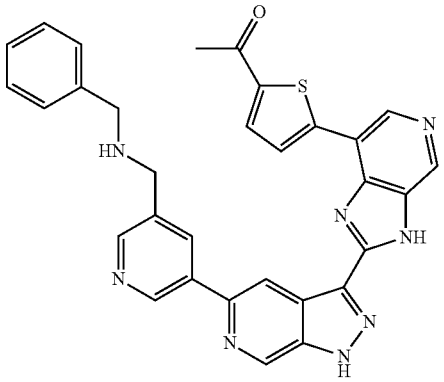
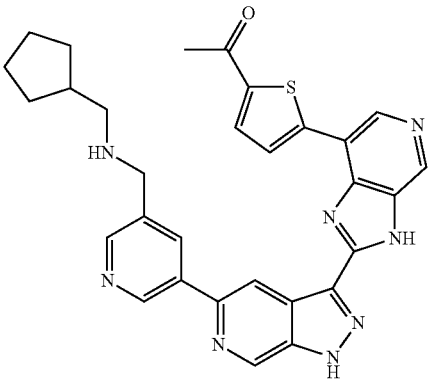
385	
386	
387	
388	

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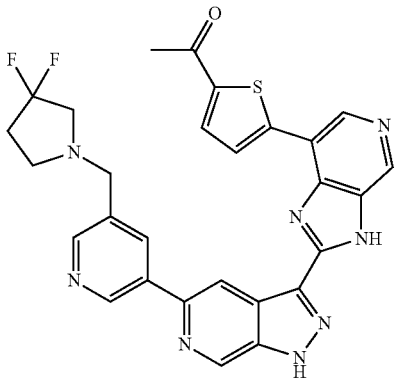
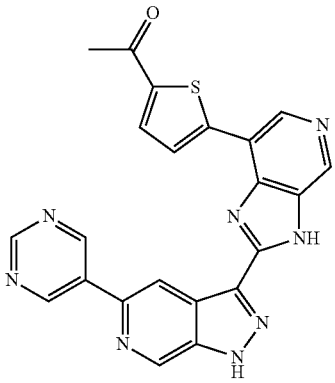
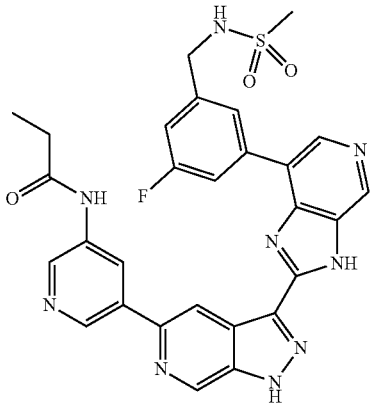
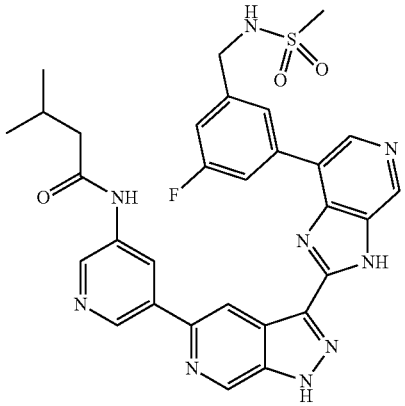
389	
390	
391	
392	

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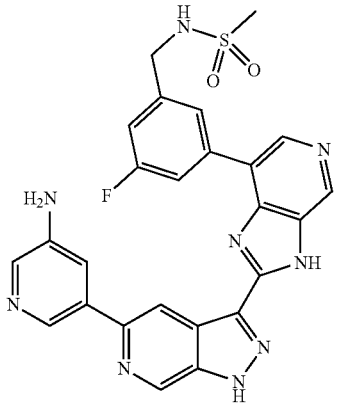
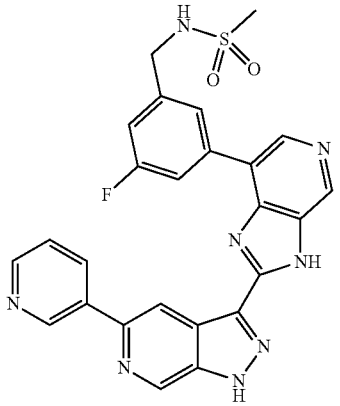
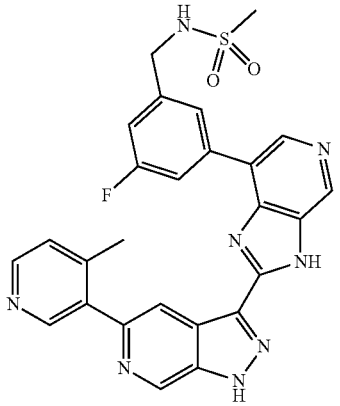
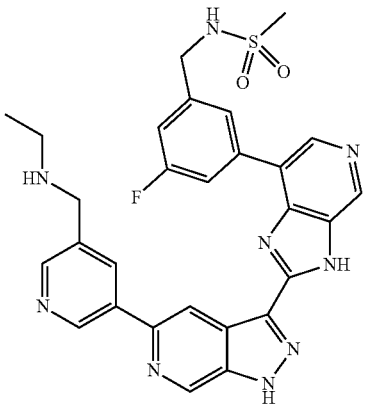
393	
394	
395	
396	

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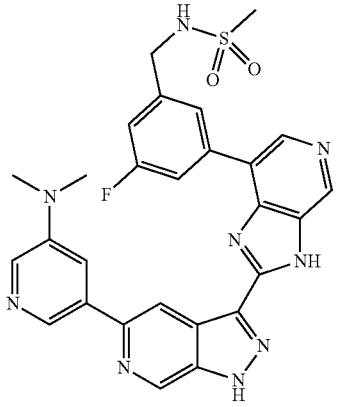
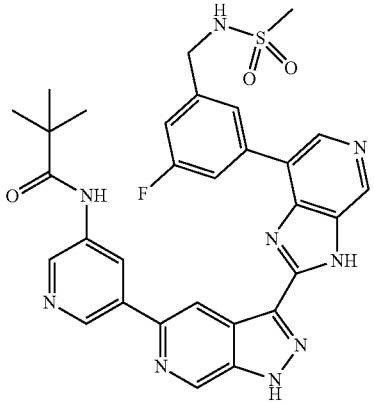
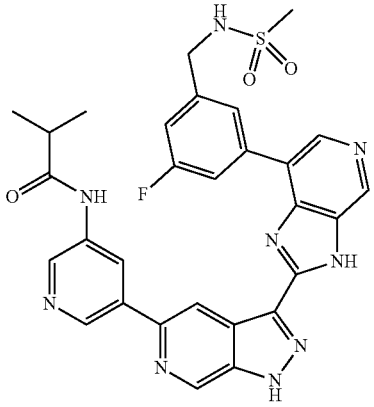
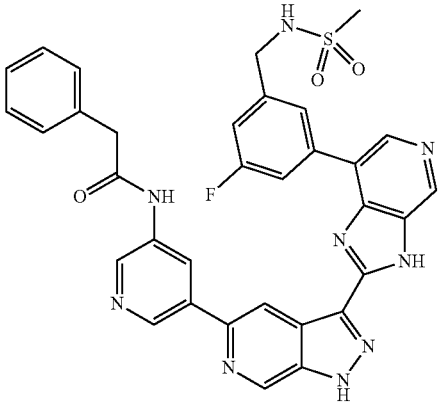
397	
398	
399	
400	

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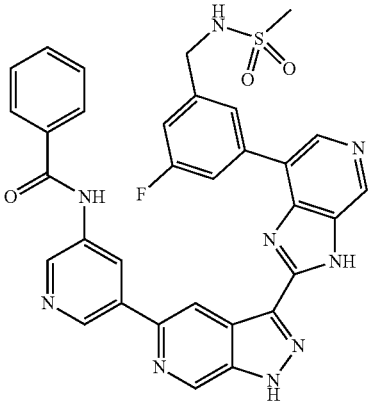
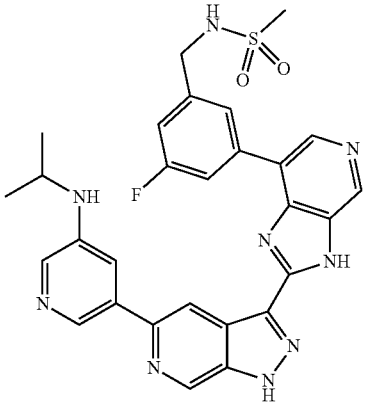
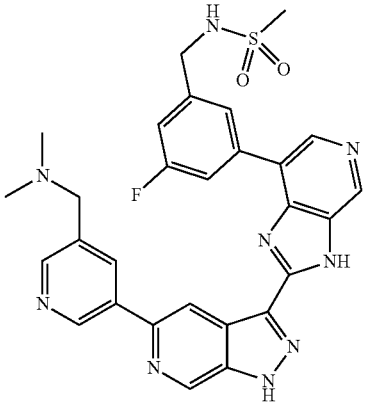
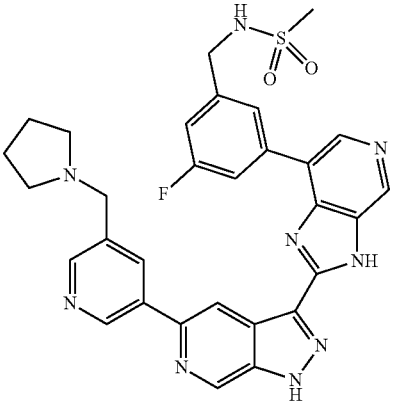
401	
402	
403	
404	

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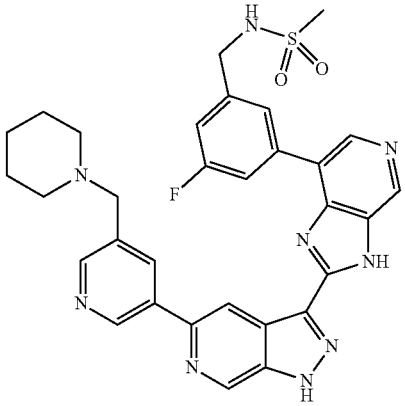
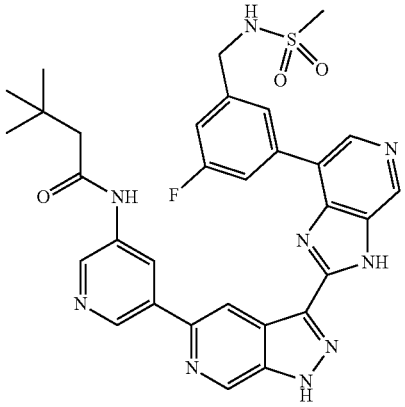
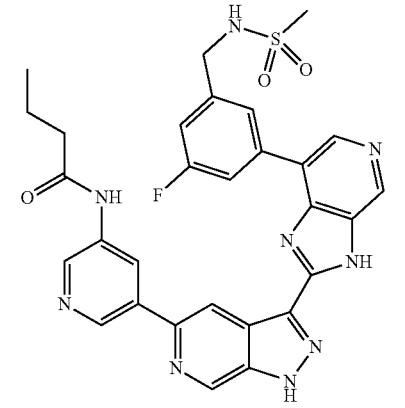
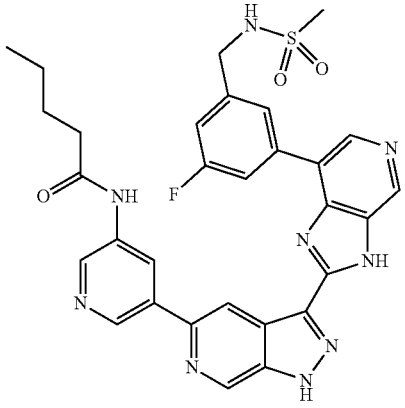
405	
406	
407	
408	

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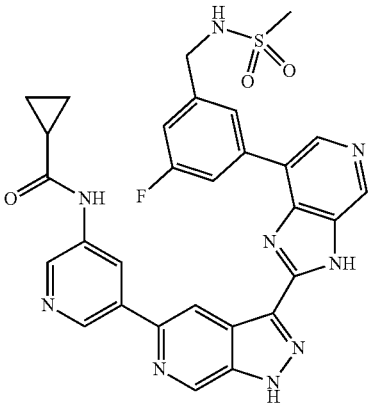
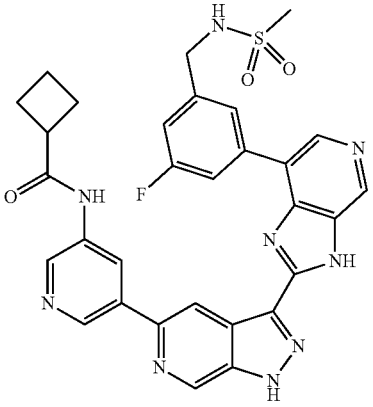
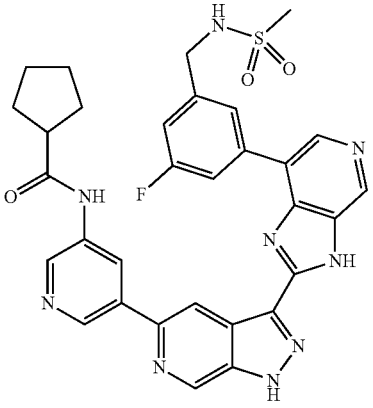
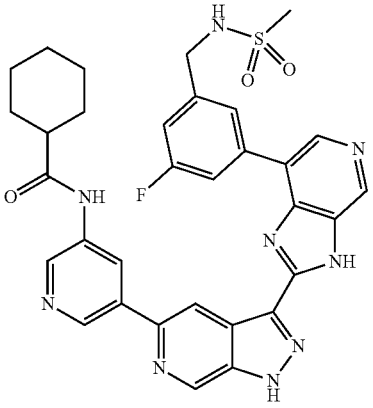
409	
410	
411	
412	

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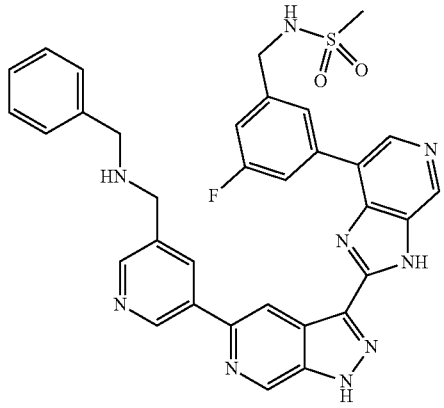
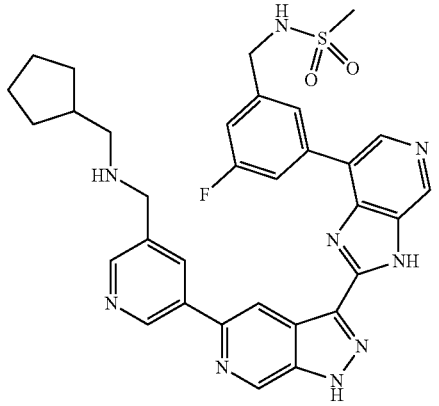
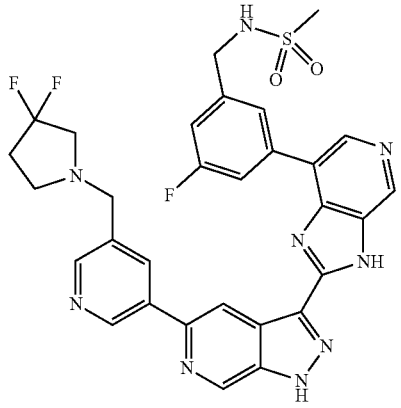
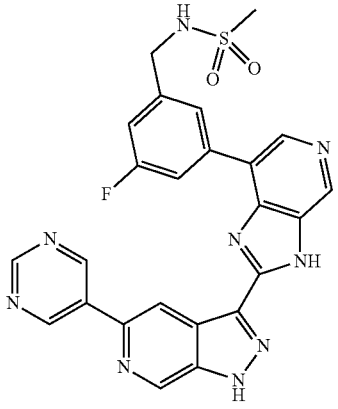
413	
414	
415	
416	

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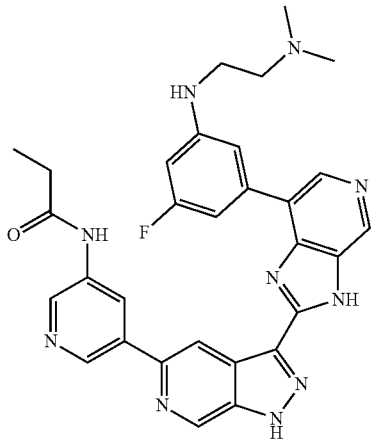
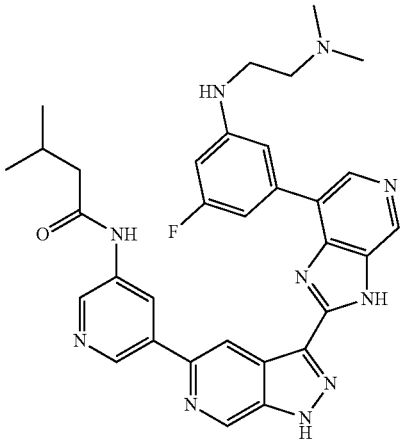
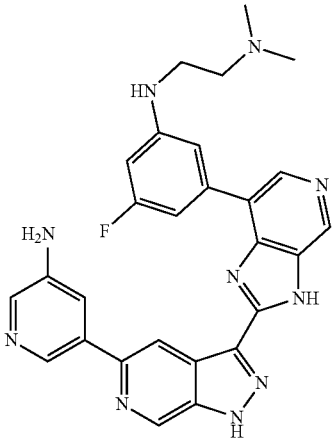
417	
418	
419	

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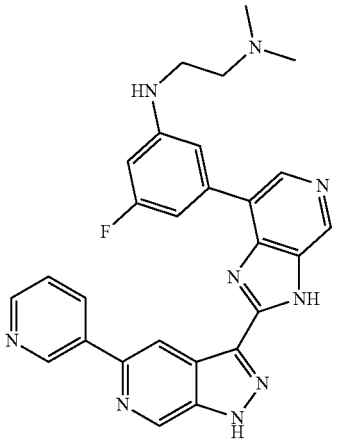
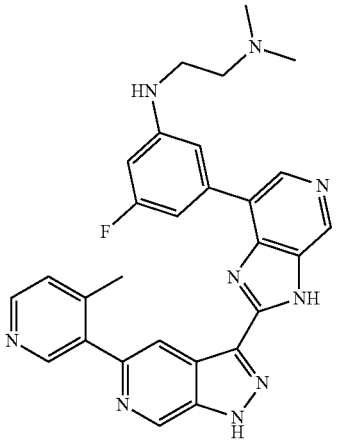
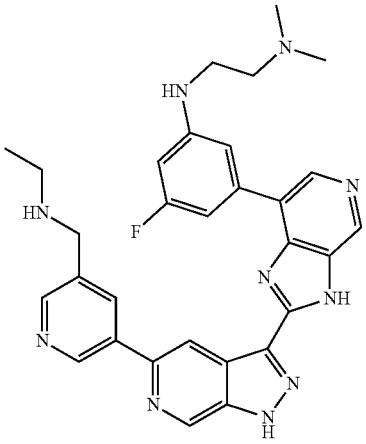
420	
421	
422	

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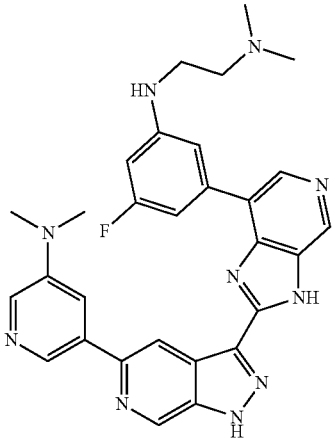
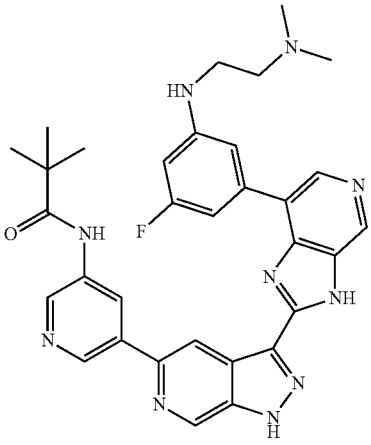
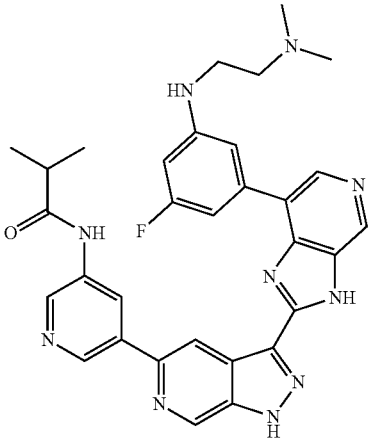
423	
424	
425	

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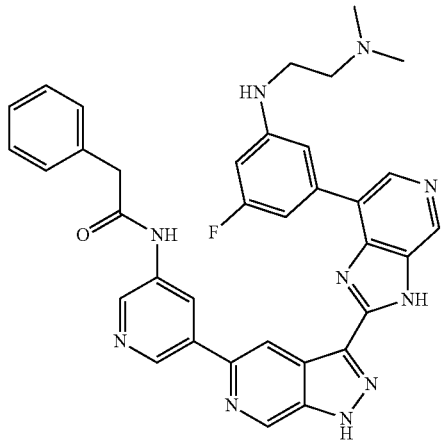
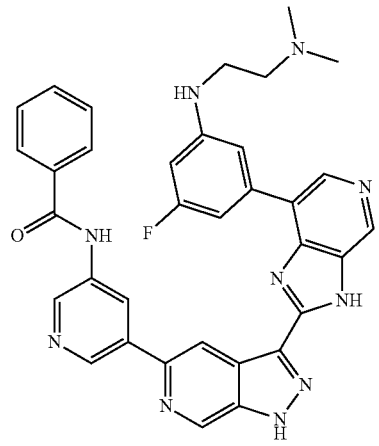
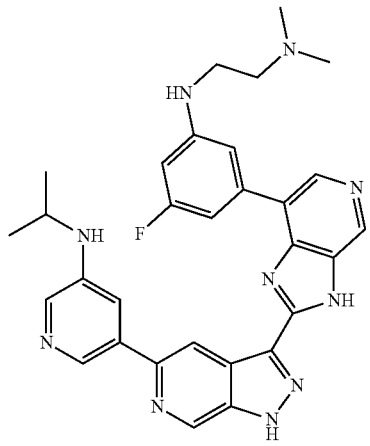
426	
427	
428	

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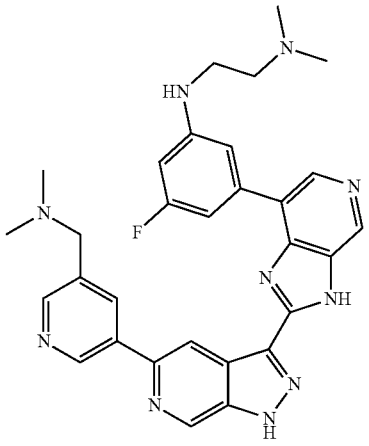
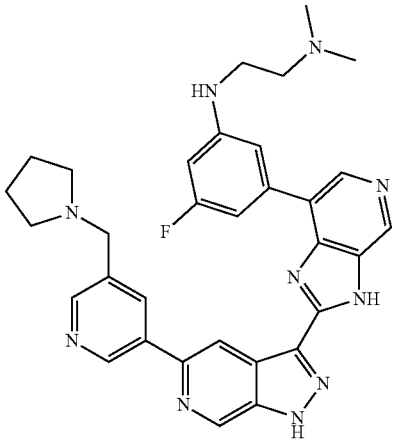
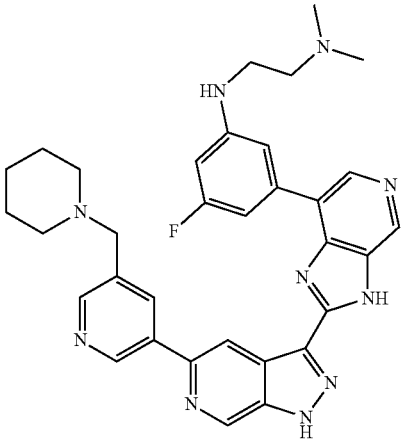
429	
430	
431	

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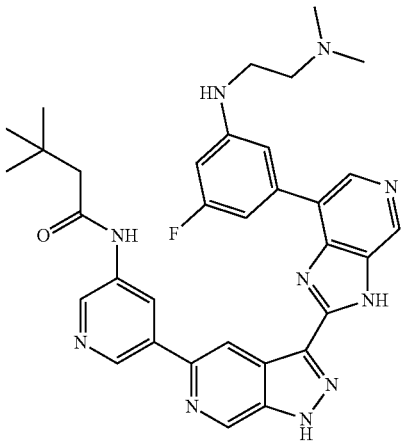
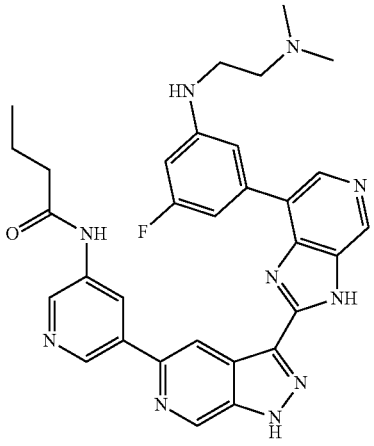
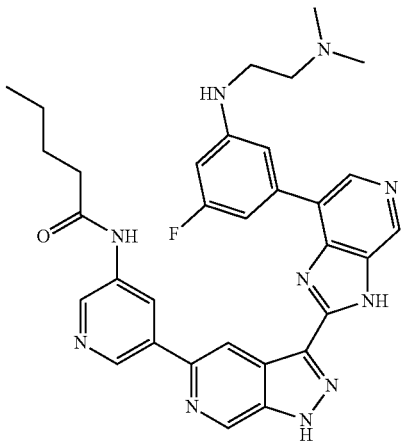
432	
433	
434	

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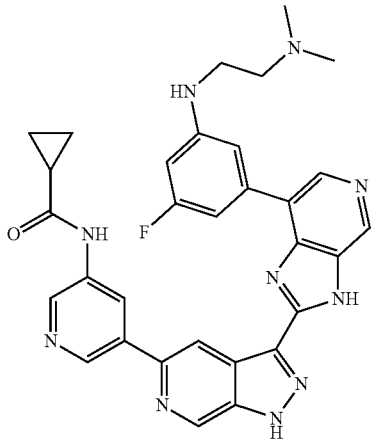
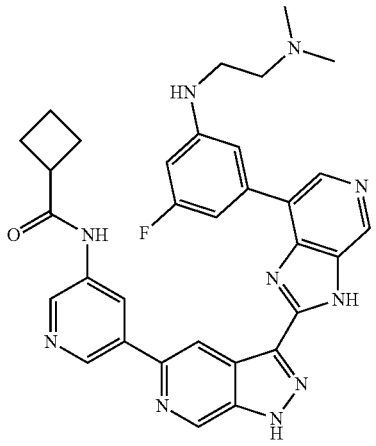
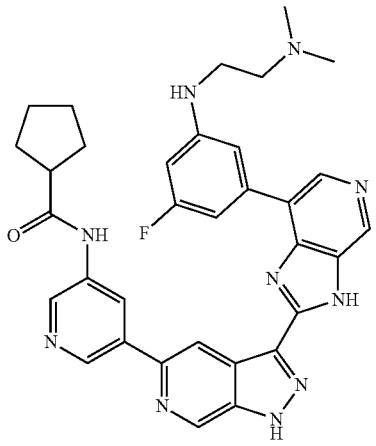
435	
436	
437	

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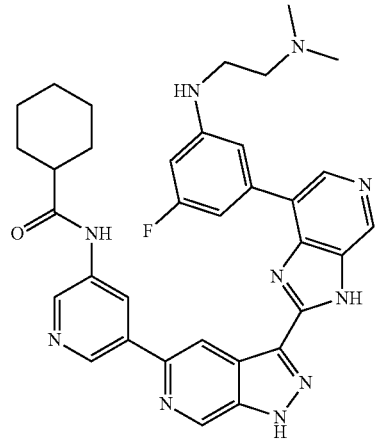
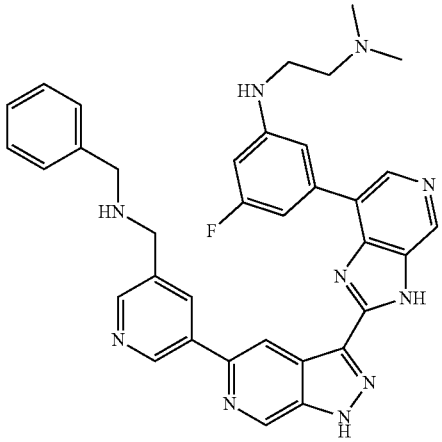
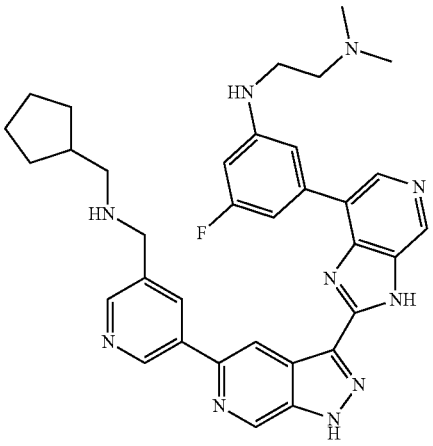
438	
439	
440	

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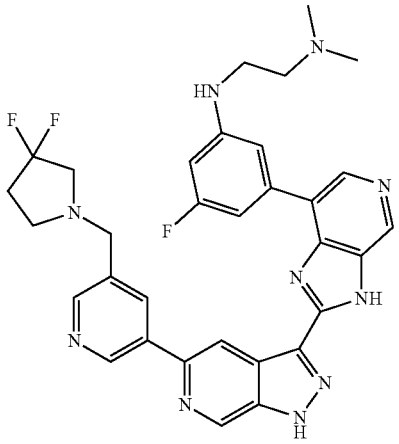
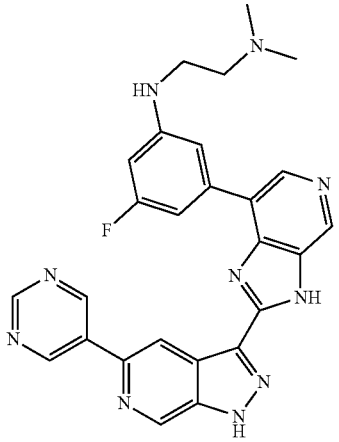
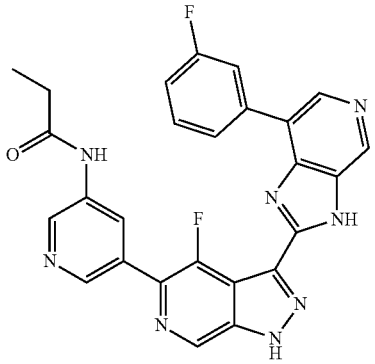
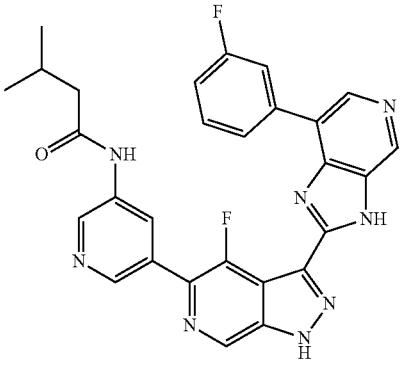
441	
442	
443	
444	

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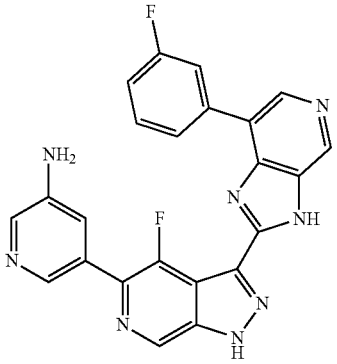
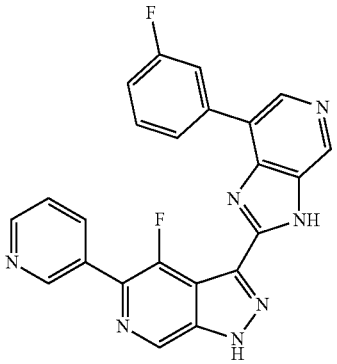
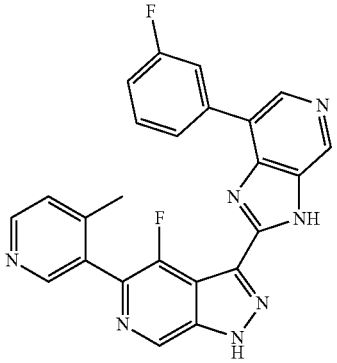
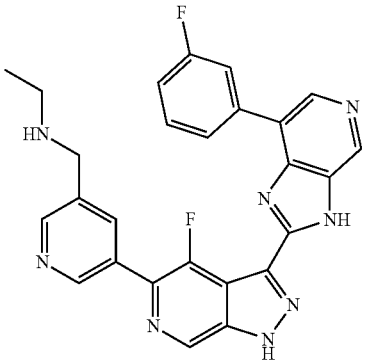
445	
446	
447	
448	

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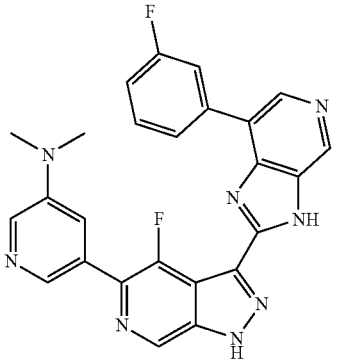
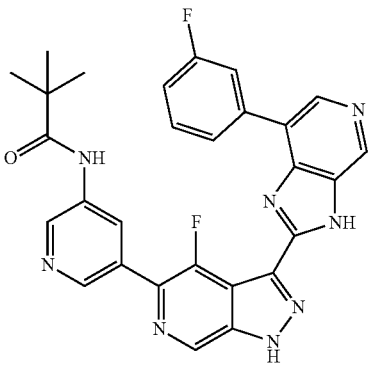
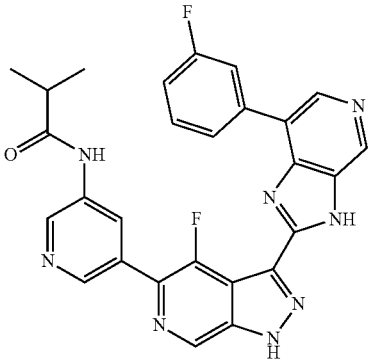
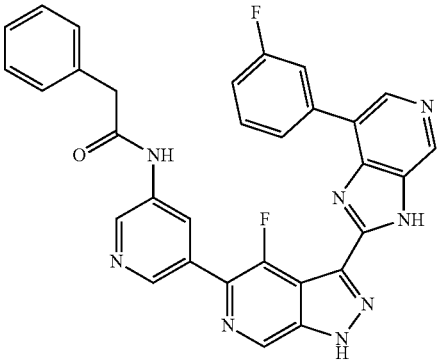
449	
450	
451	
452	

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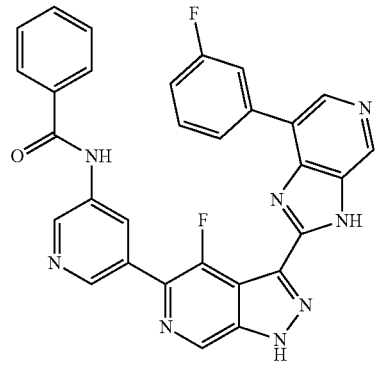
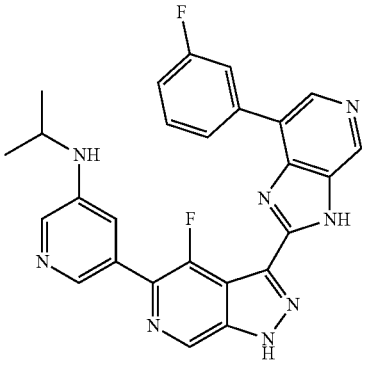
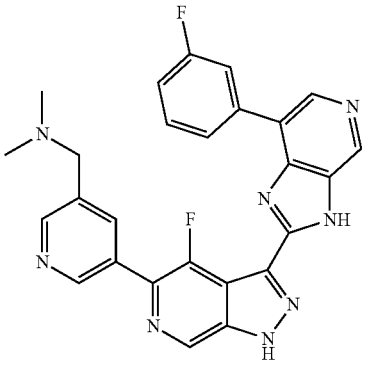
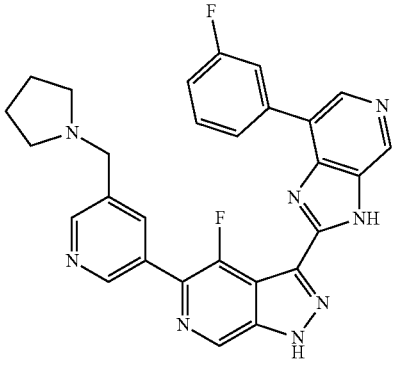
453	
454	
455	
456	

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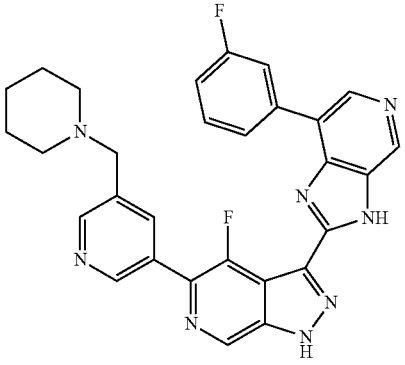
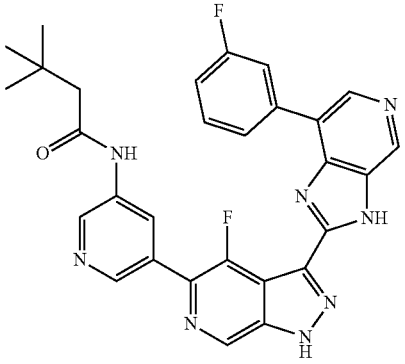
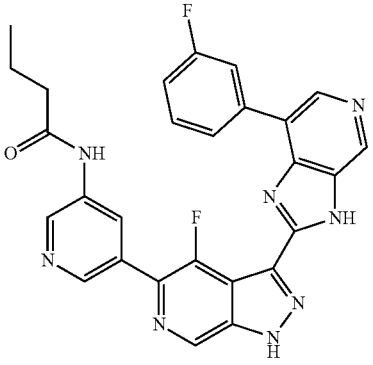
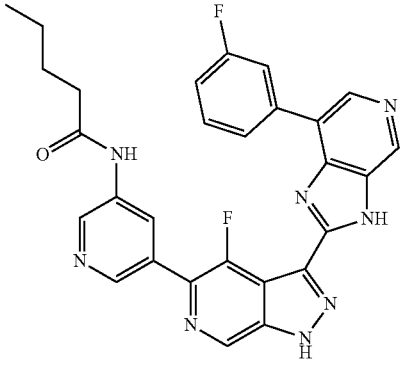
457	
458	
459	
460	

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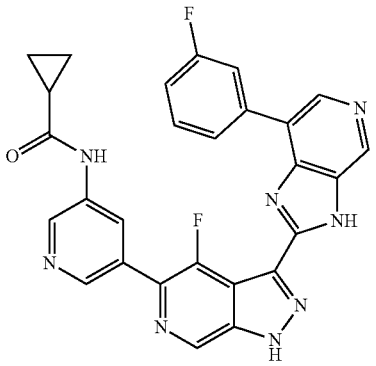
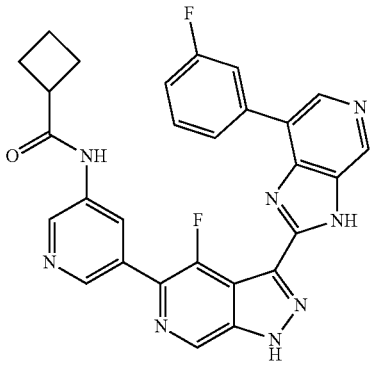
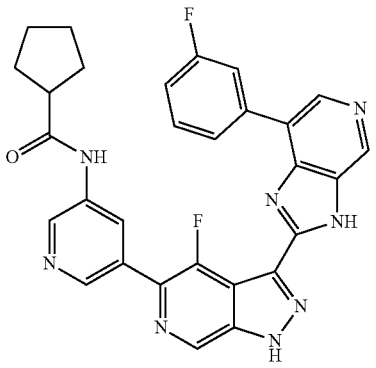
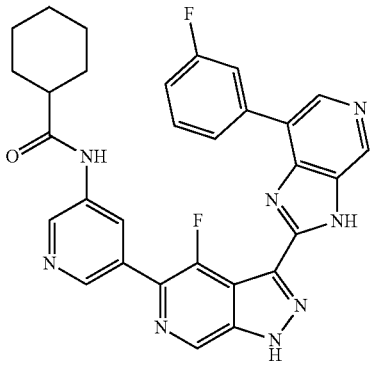
461	
462	
463	
464	

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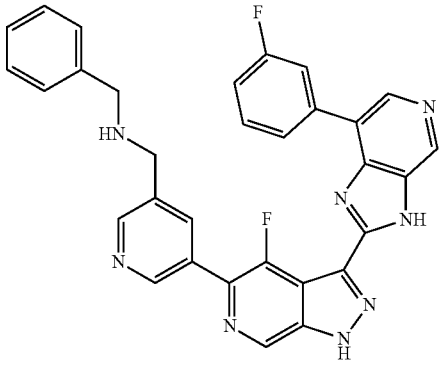
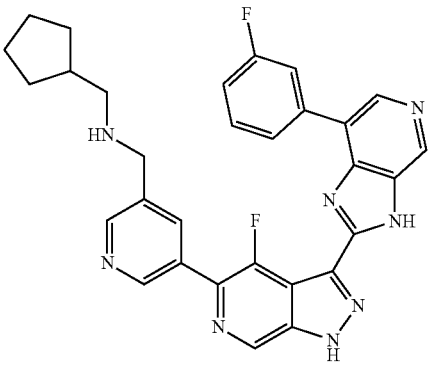
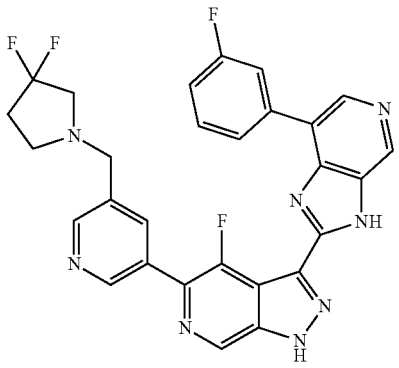
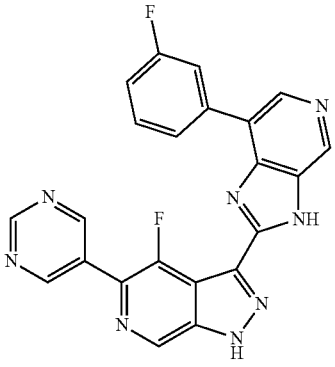
465	
466	
467	
468	

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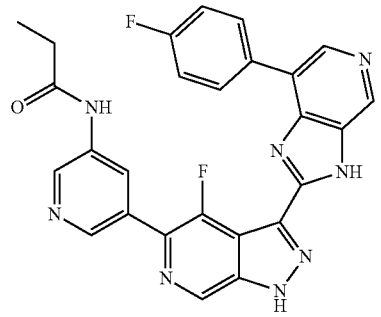
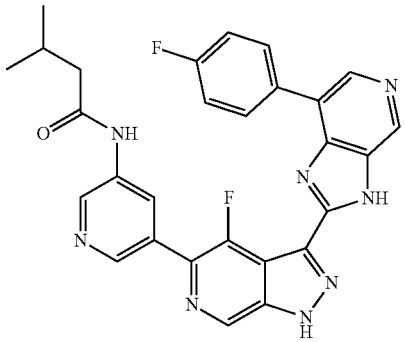
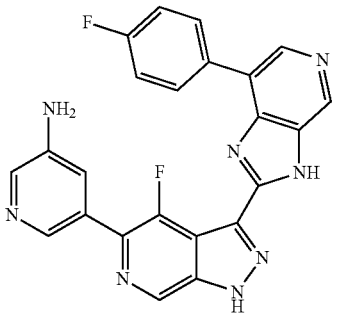
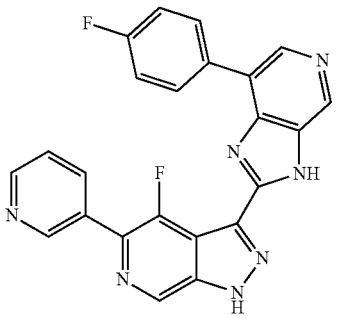
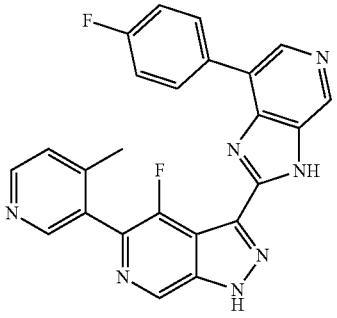
469	
470	
471	
472	
473	

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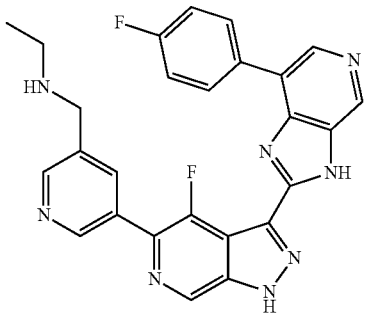
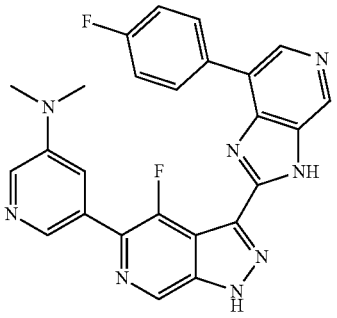
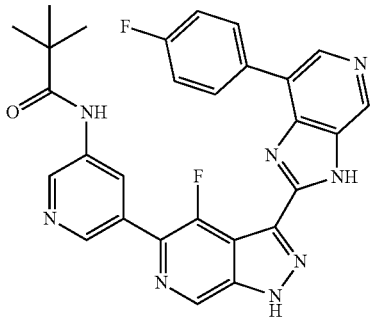
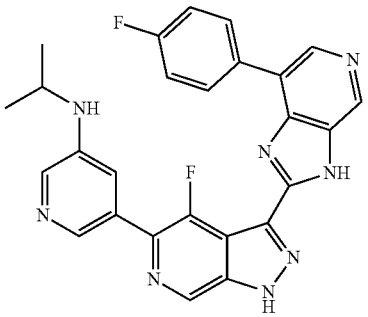
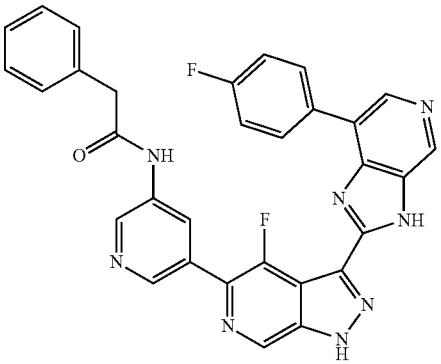
474	
475	
476	
477	
478	

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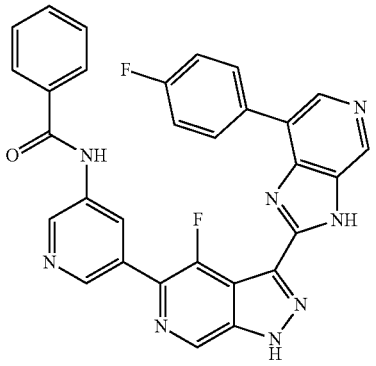
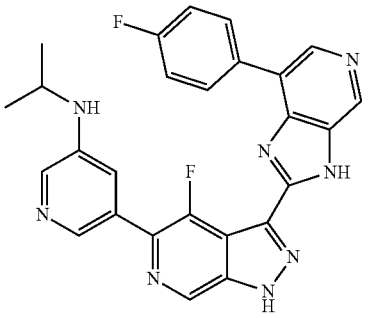
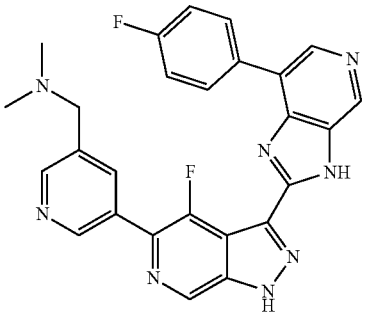
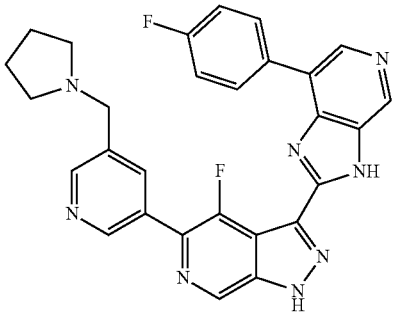
479	
480	
481	
482	

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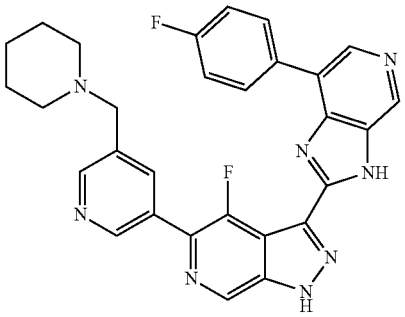
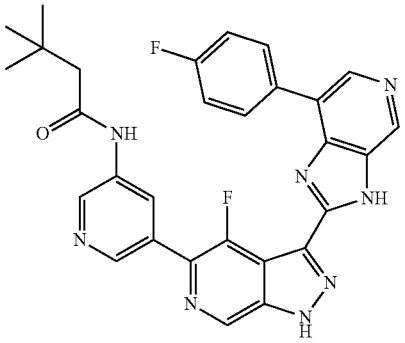
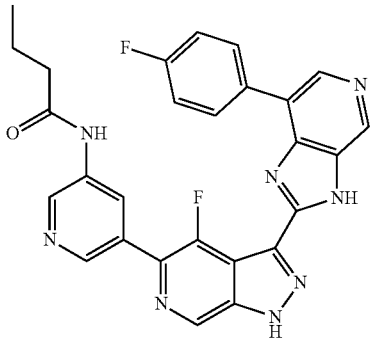
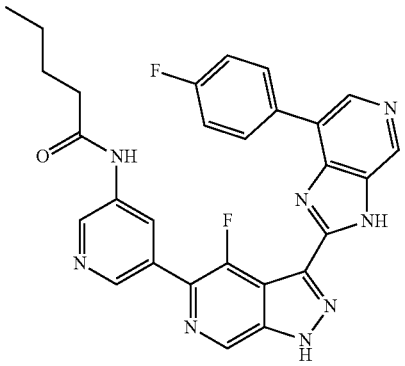
483	
484	
485	
486	

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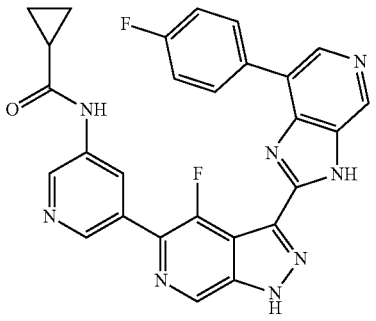
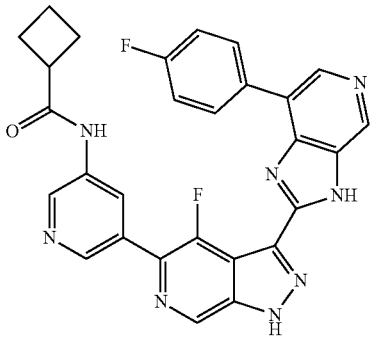
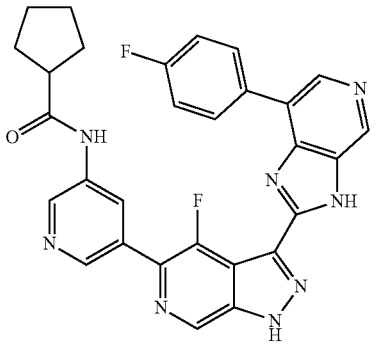
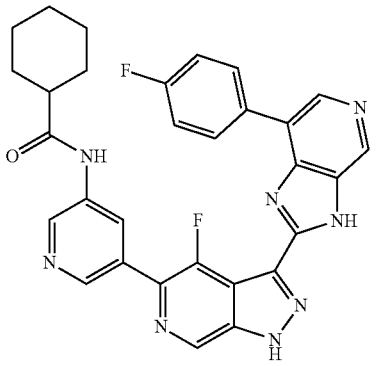
487	
488	
489	
490	

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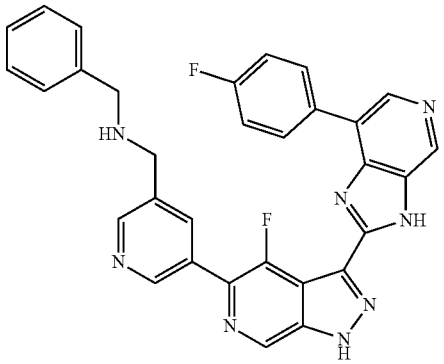
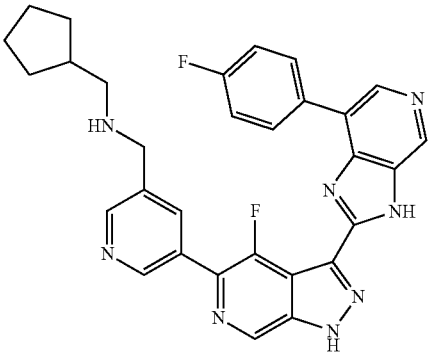
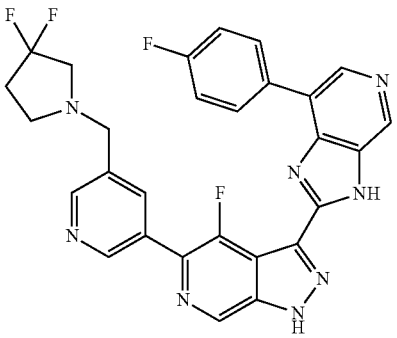
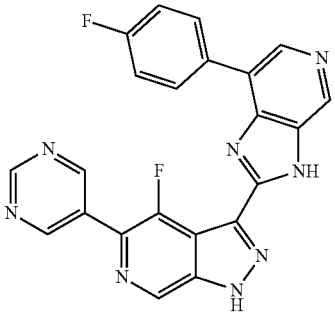
491	
492	
493	
494	

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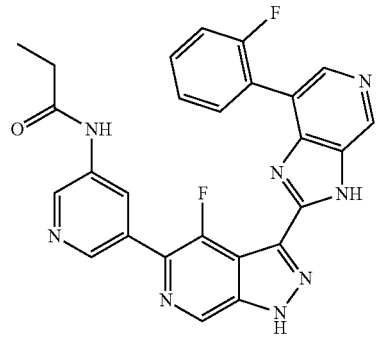
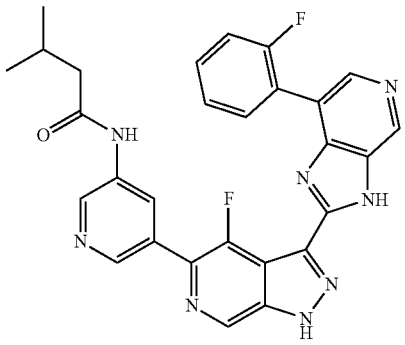
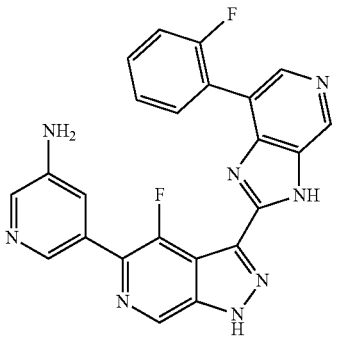
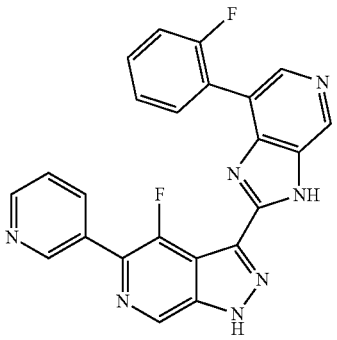
495	
496	
497	
498	

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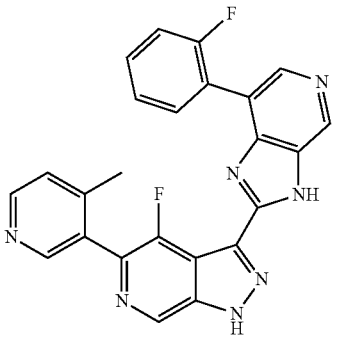
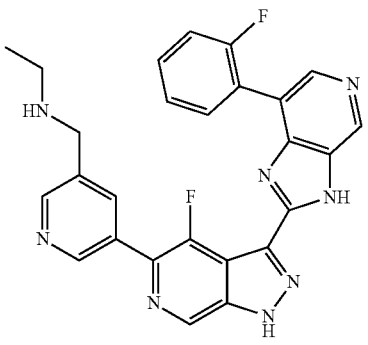
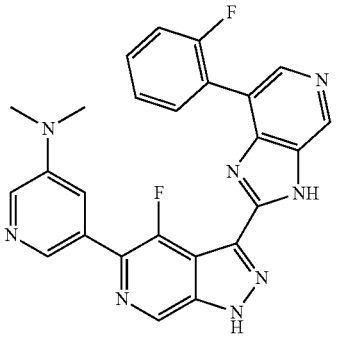
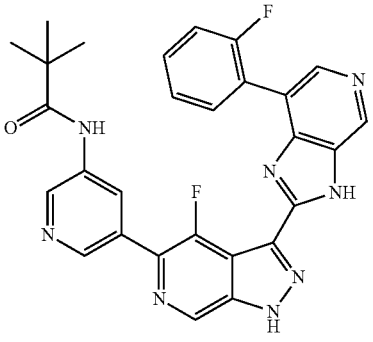
499	
500	
501	
502	

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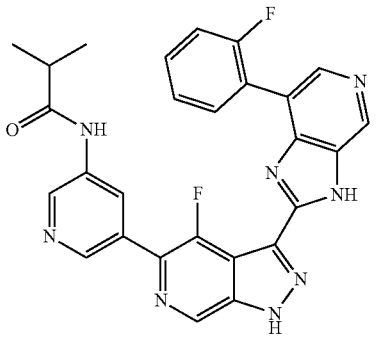
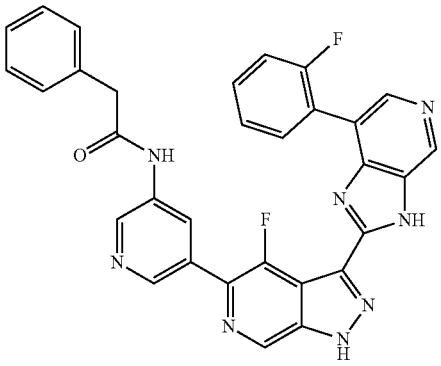
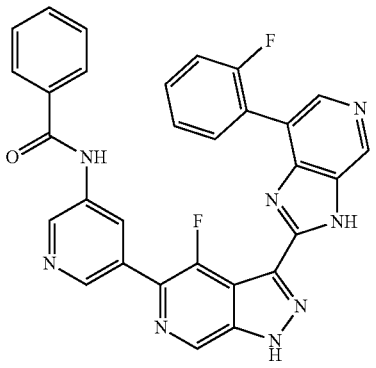
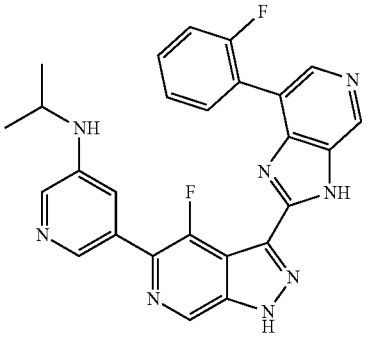
503	
504	
505	
506	

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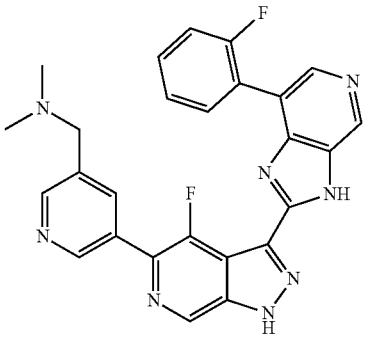
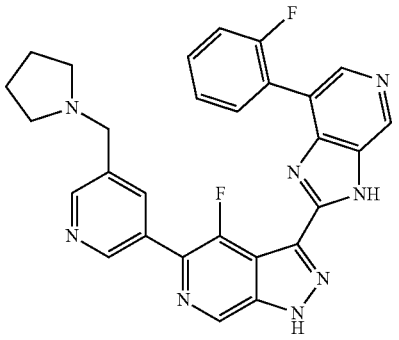
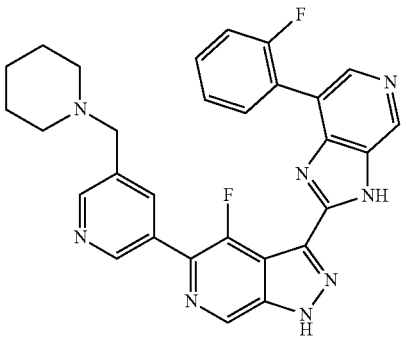
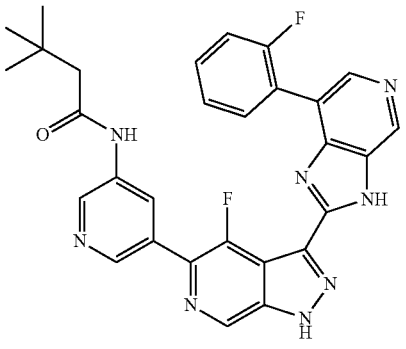
507	
508	
509	
510	

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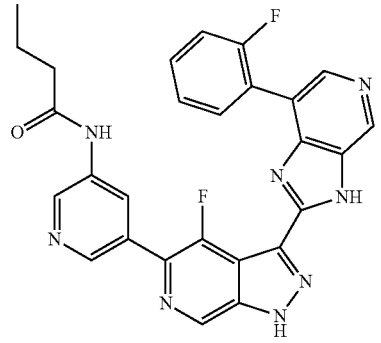
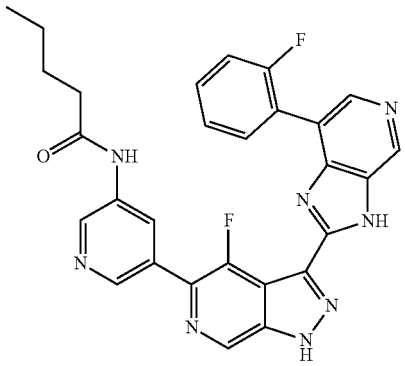
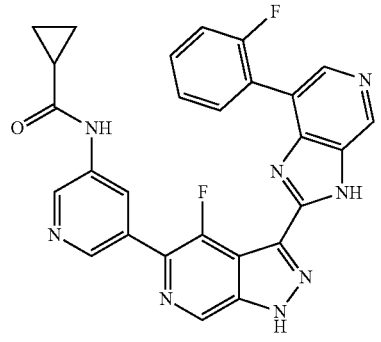
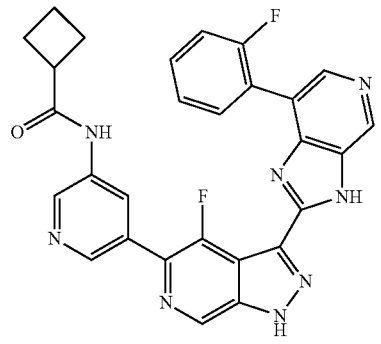
511	
512	
513	
514	

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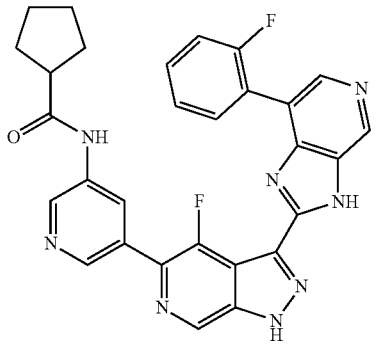
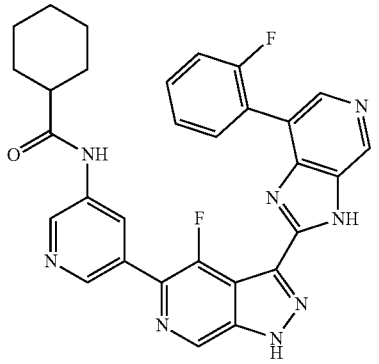
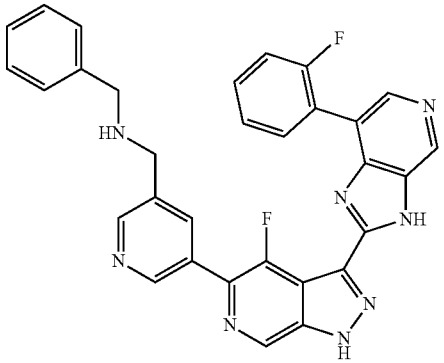
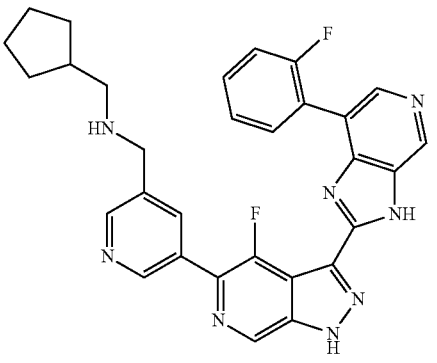
515	
516	
517	
518	

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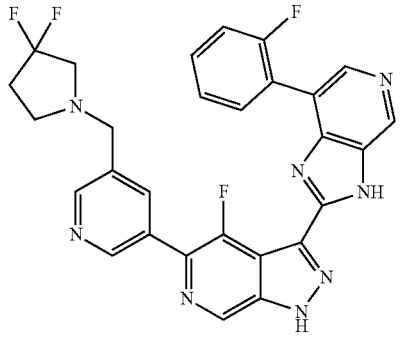
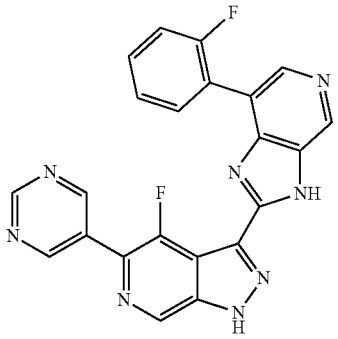
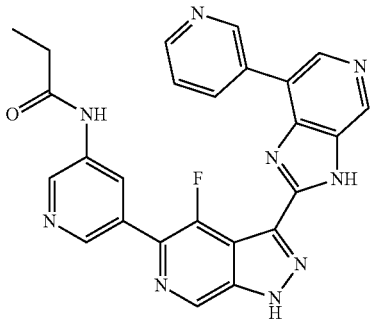
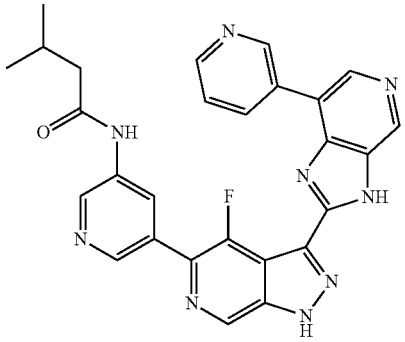
519	
520	
521	
522	

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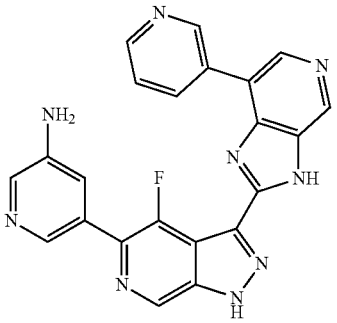
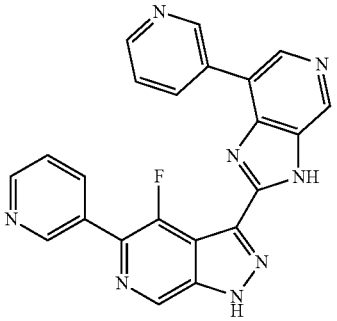
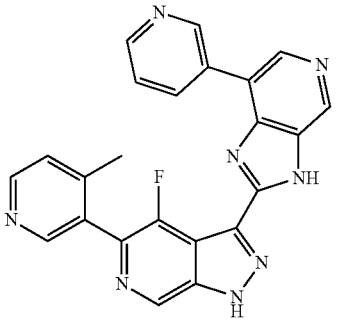
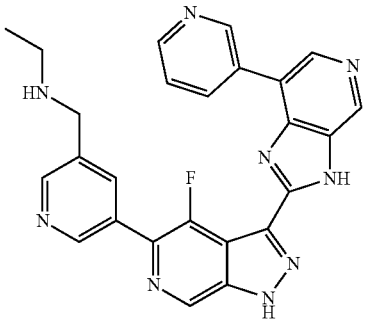
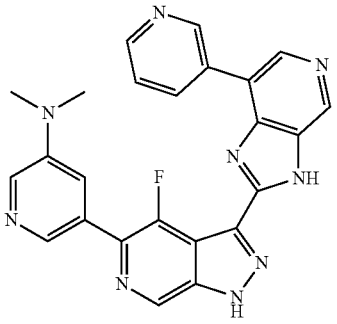
523	
524	
525	
526	
527	

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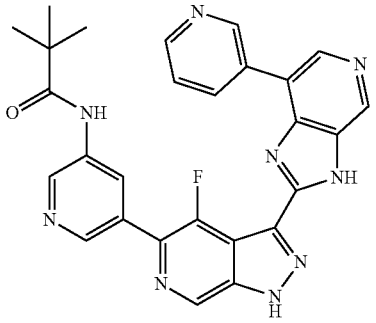
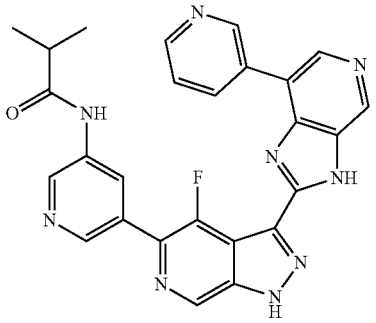
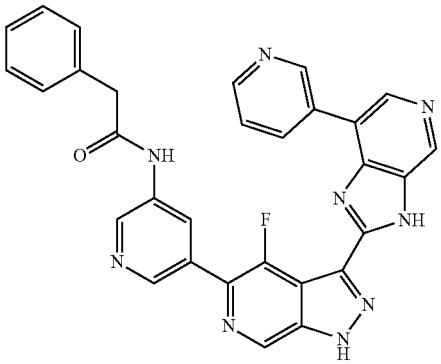
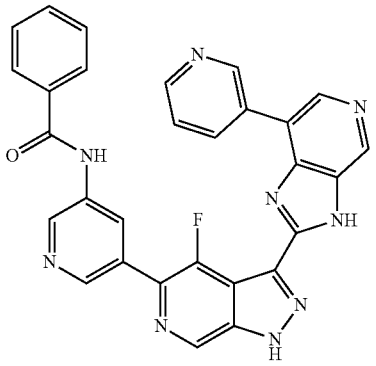
528	
529	
530	
531	

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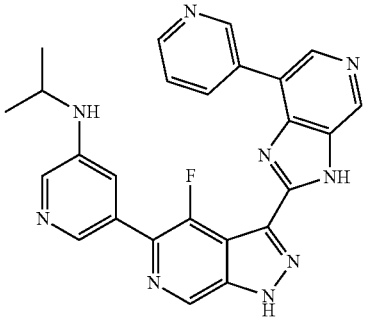
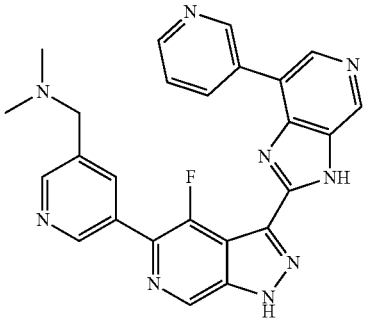
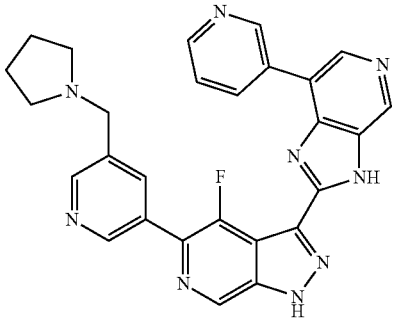
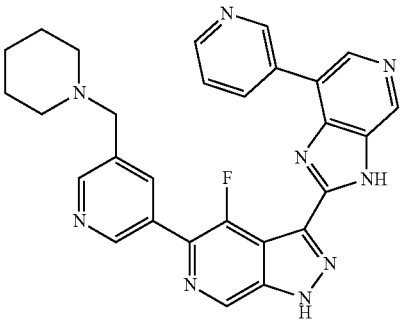
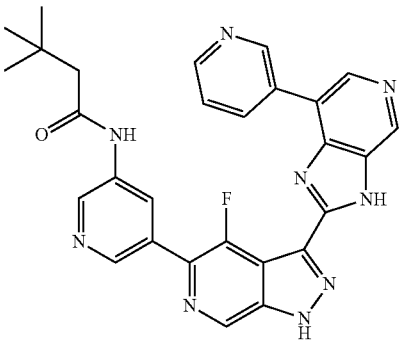
532	
533	
534	
535	
536	

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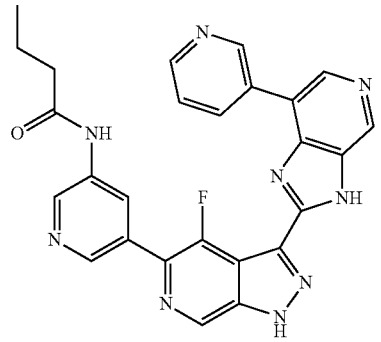
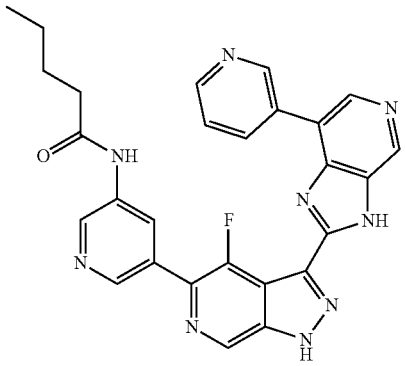
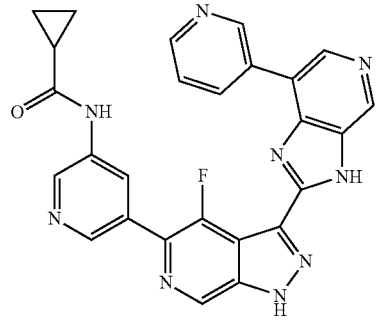
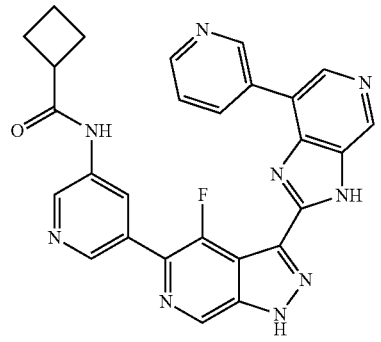
537	
538	
539	
540	

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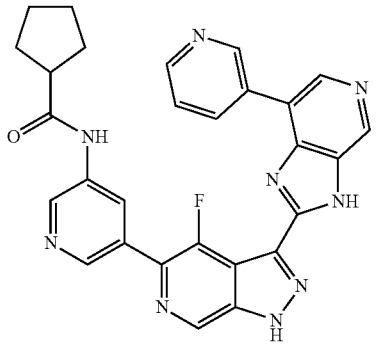
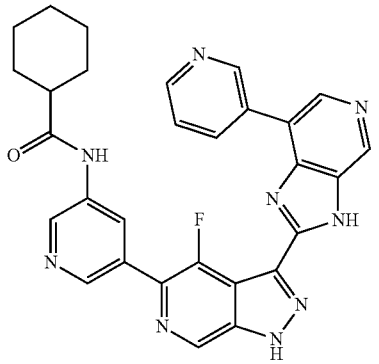
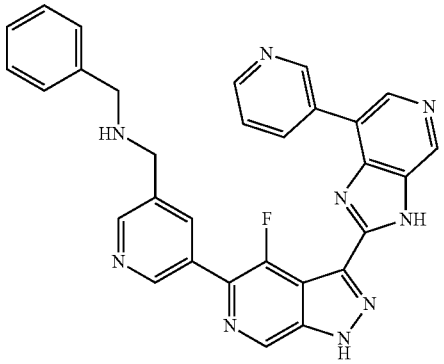
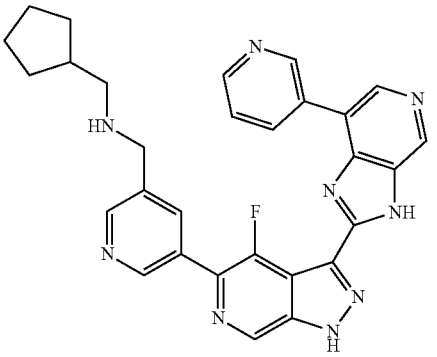
541	
542	
543	
544	

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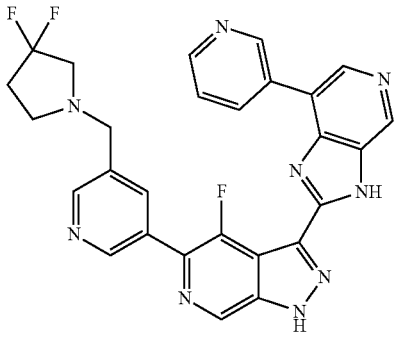
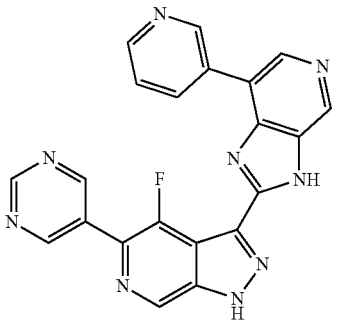
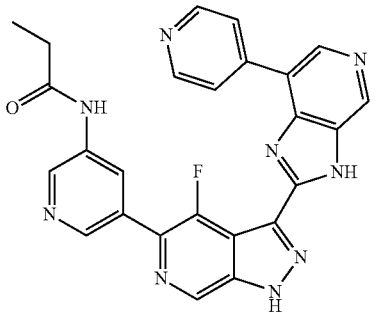
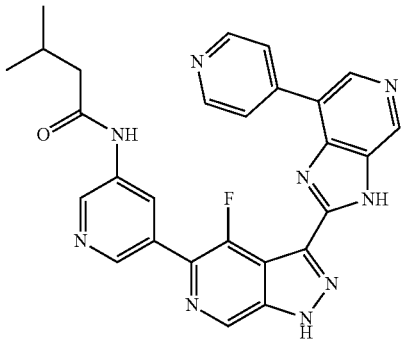
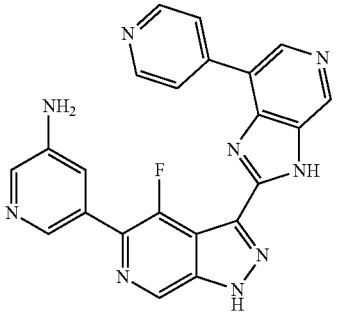
545	
546	
547	
548	
549	

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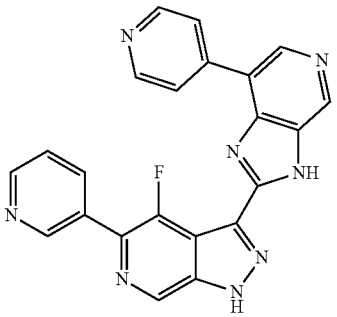
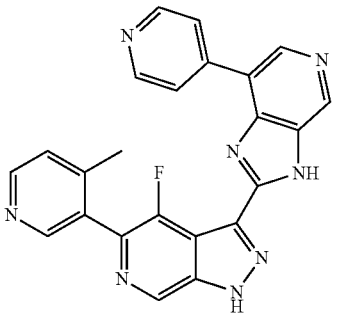
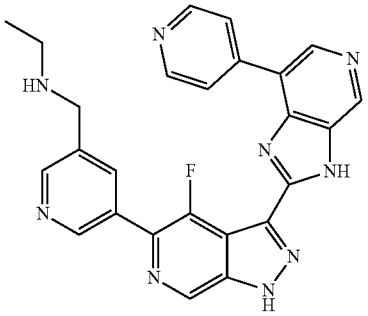
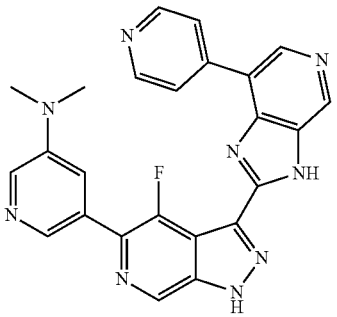
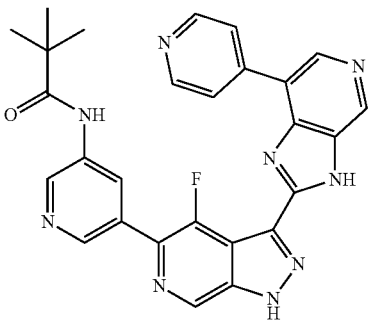
550	
551	
552	
553	
554	

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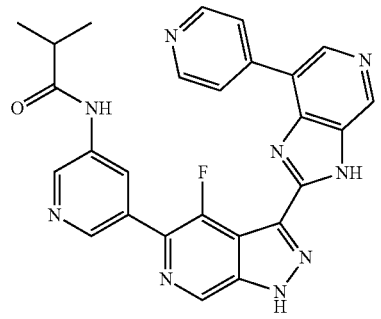
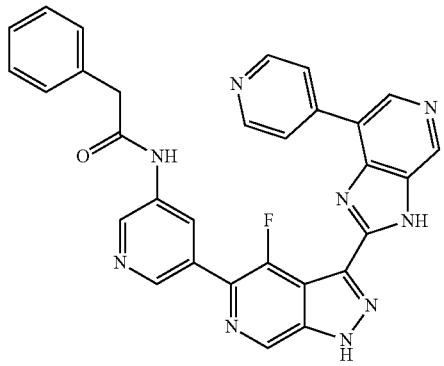
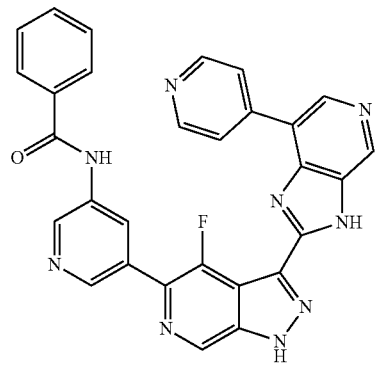
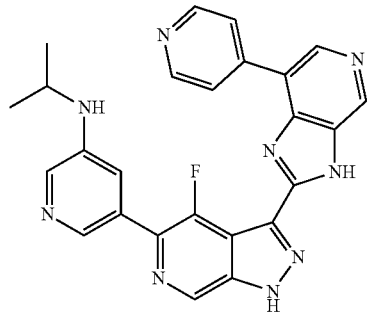
555	
556	
557	
558	

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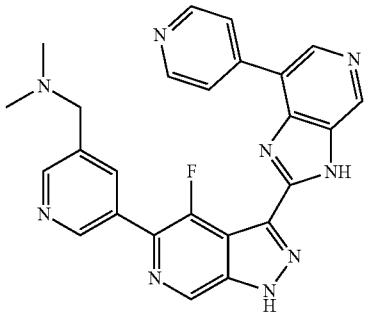
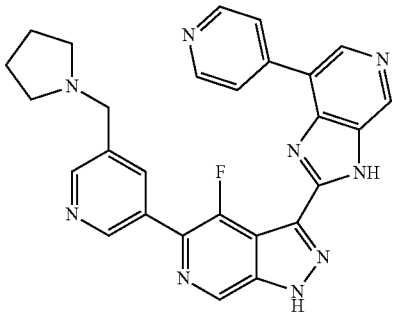
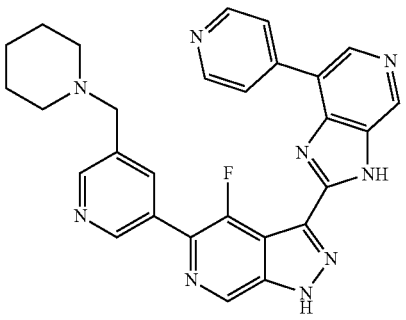
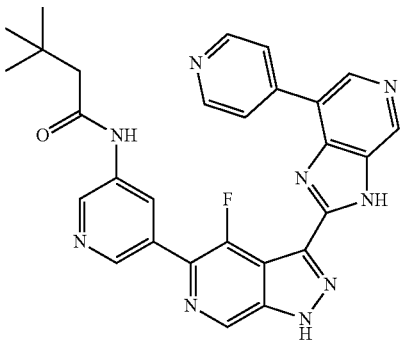
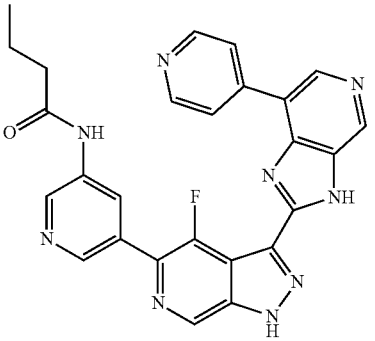
559	
560	
561	
562	
563	

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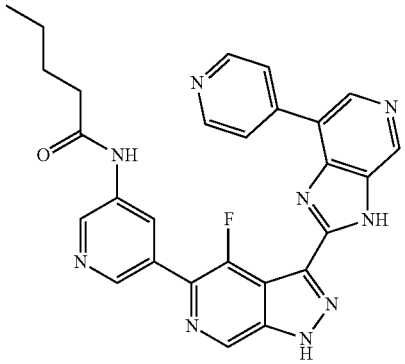
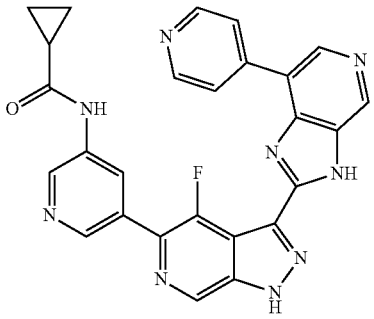
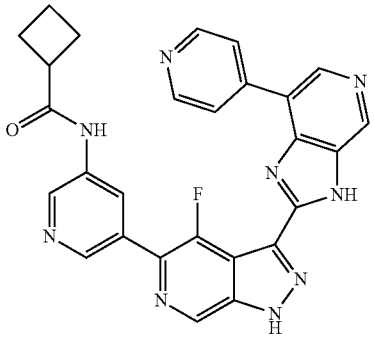
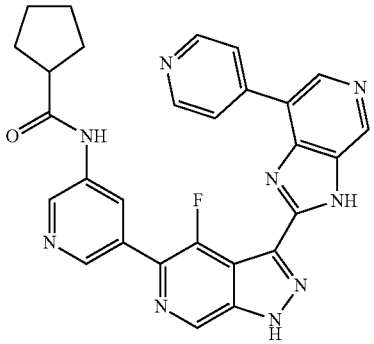
564	
565	
566	
567	

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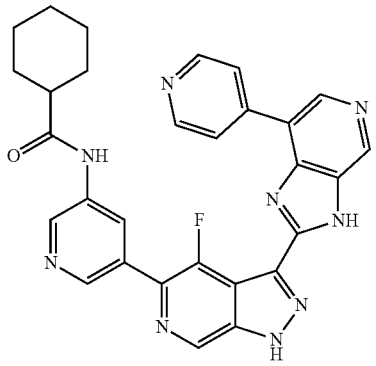
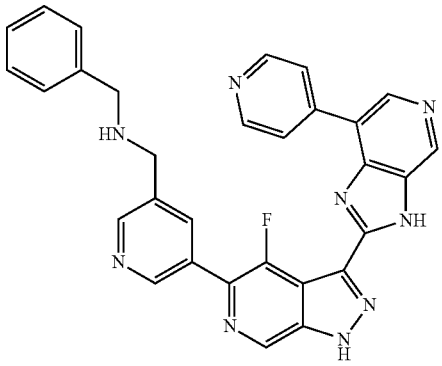
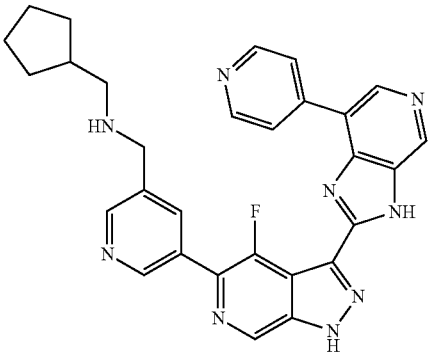
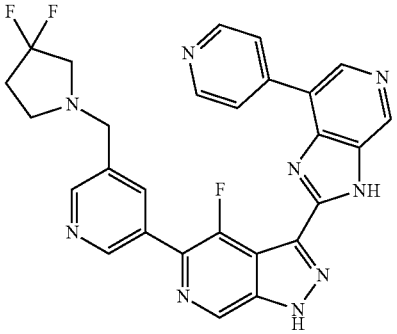
568	
569	
570	
571	

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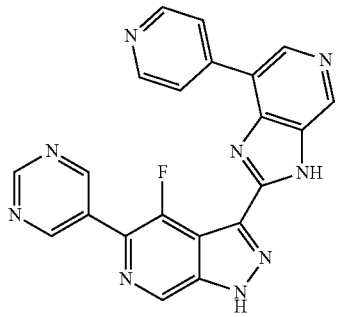
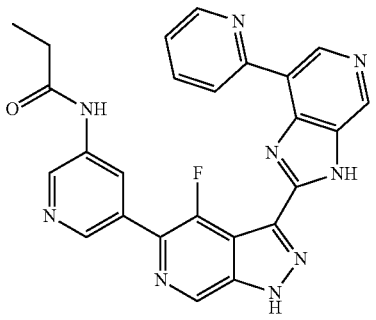
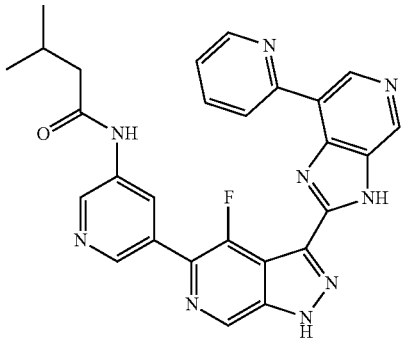
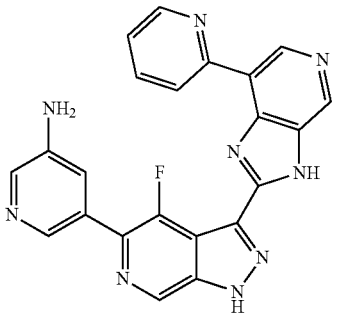
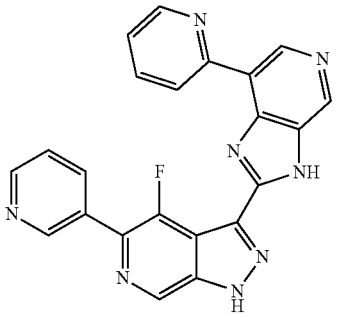
572	
573	
574	
575	
576	

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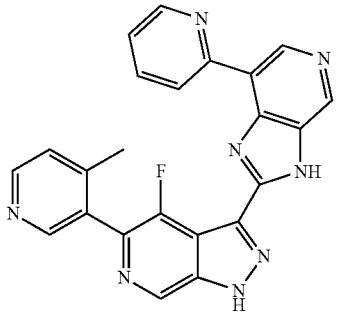
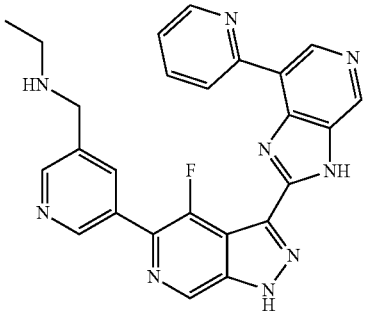
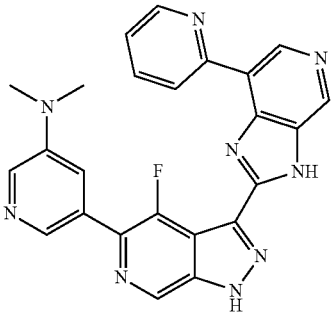
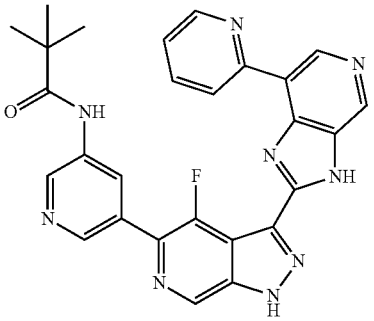
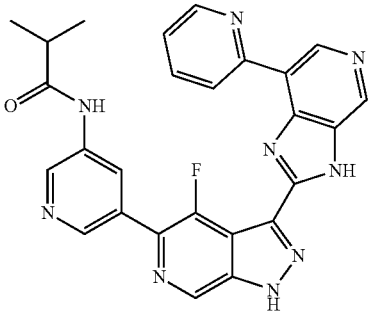
577	
578	
579	
580	
581	

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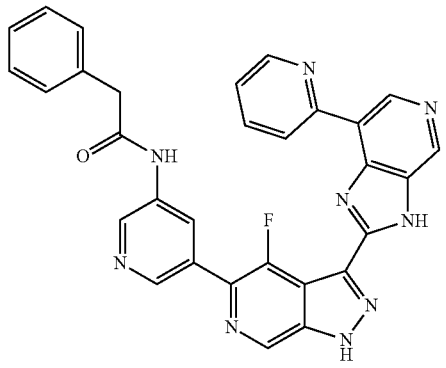

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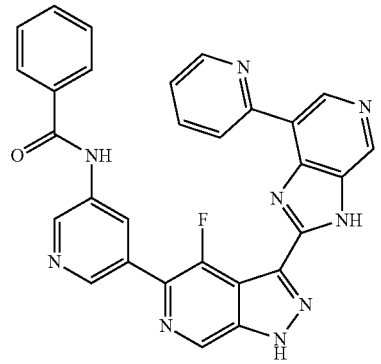

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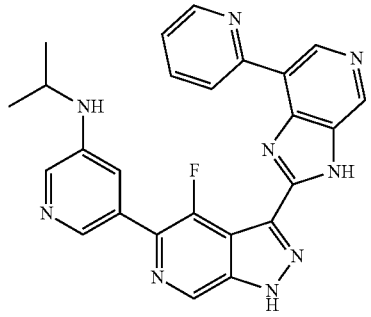

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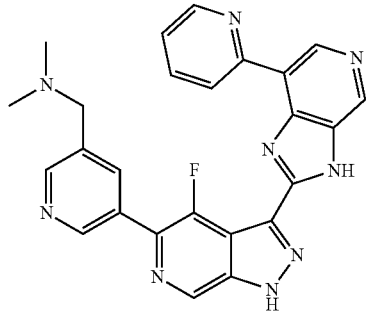

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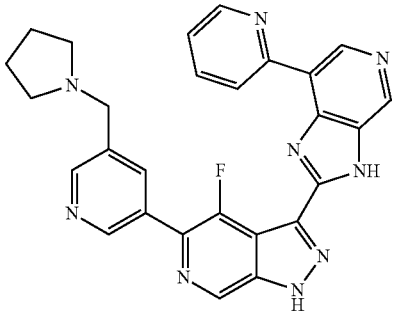

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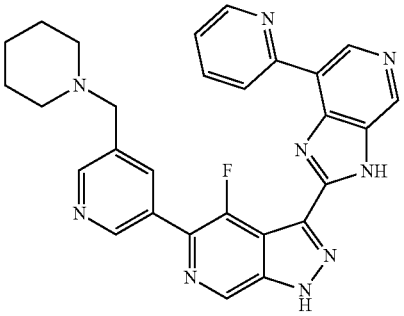

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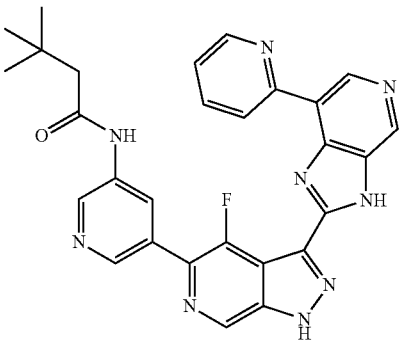

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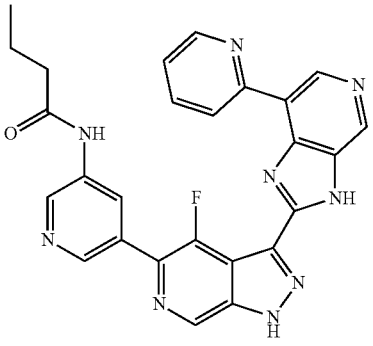

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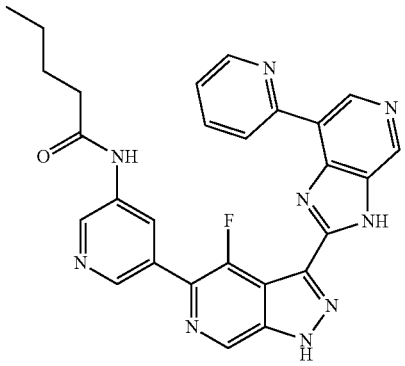
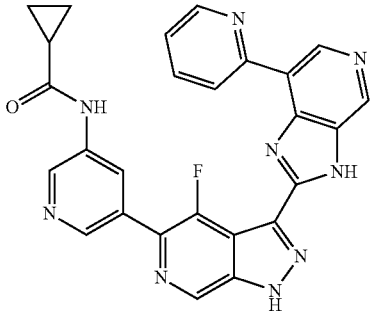
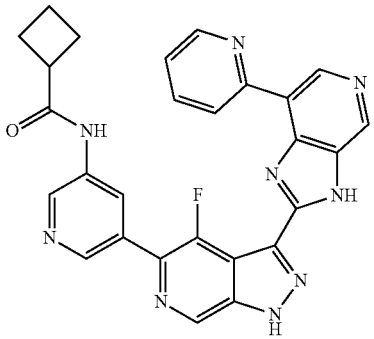
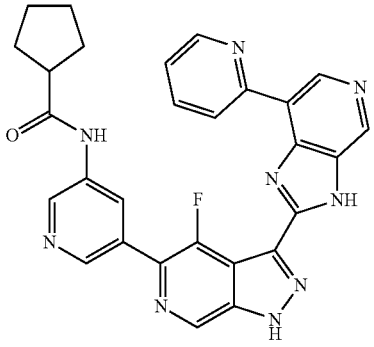
590	
591	
592	
593	

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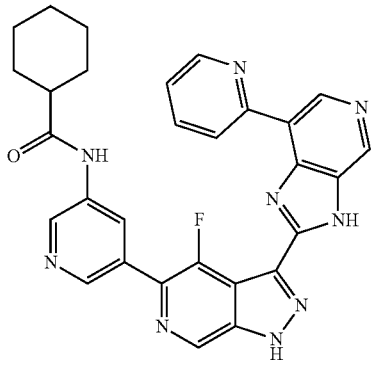
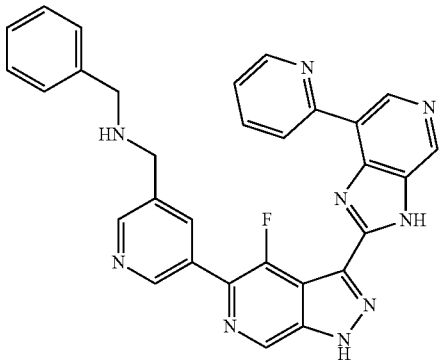
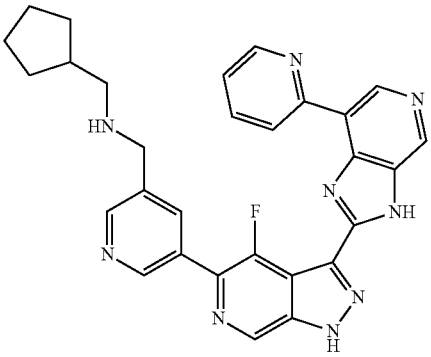
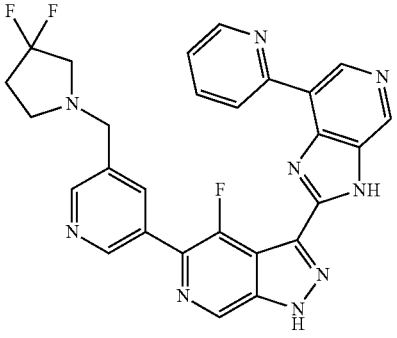
594	
595	
596	
597	

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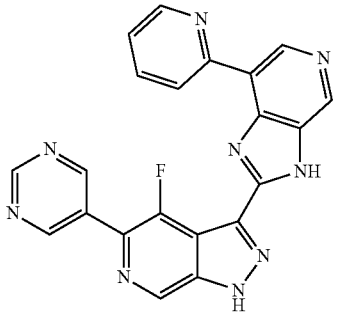
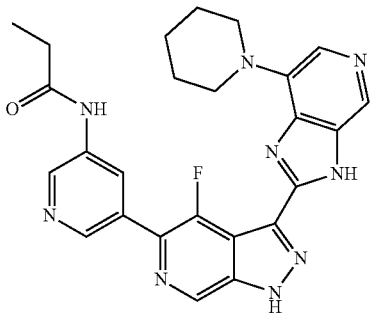
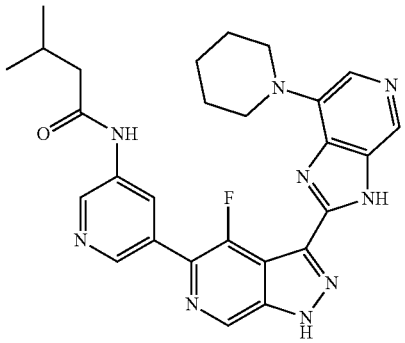
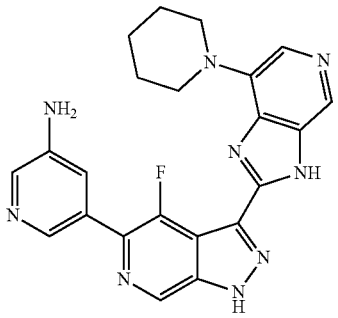
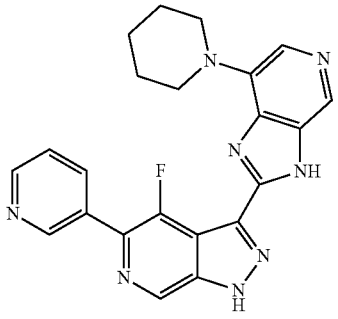
598	
599	
600	
601	
602	

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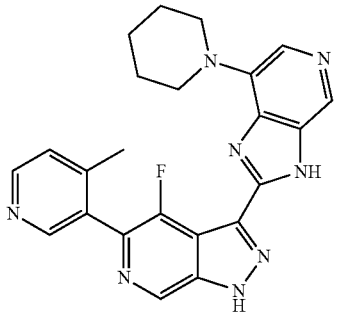
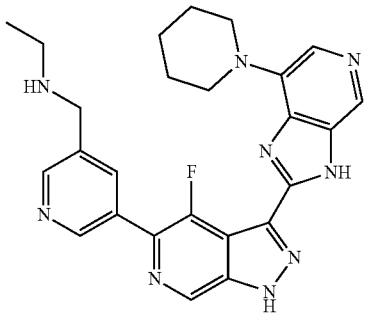
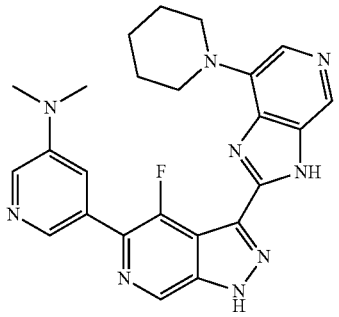
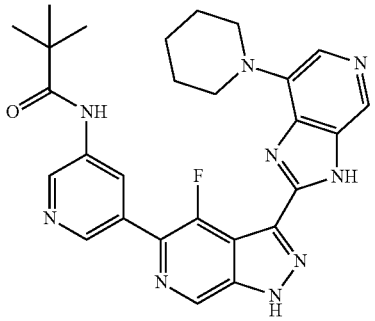
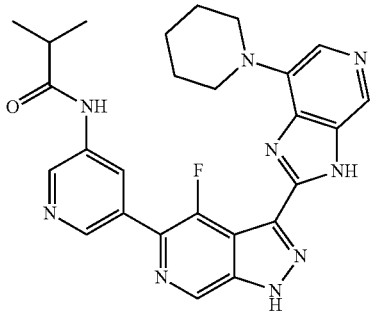
603	
604	
605	
606	
607	

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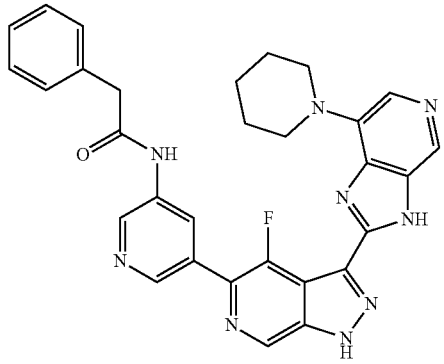
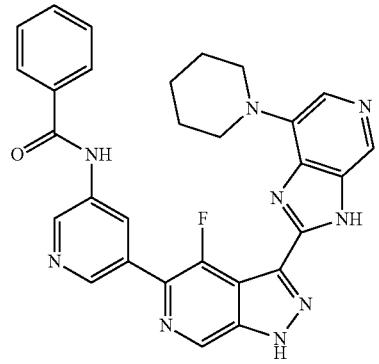
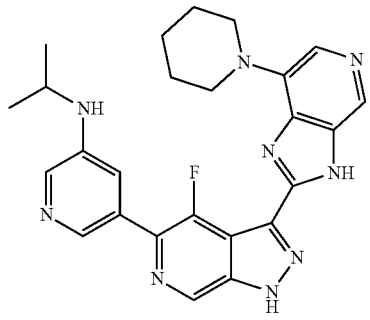
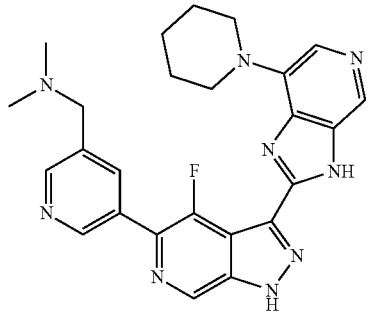
608	
609	
610	
611	

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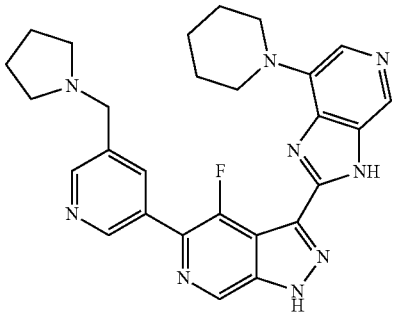
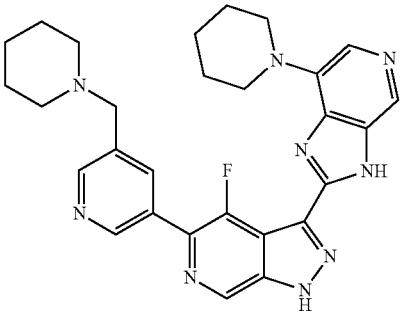
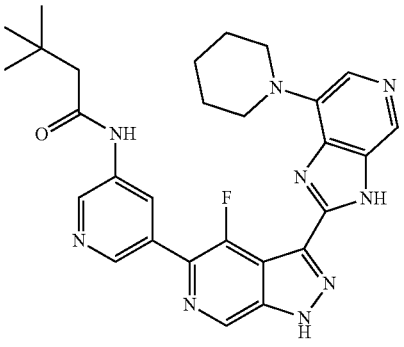
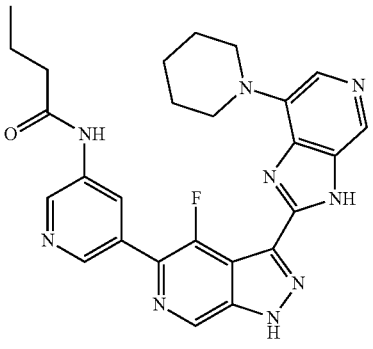
612	
613	
614	
615	

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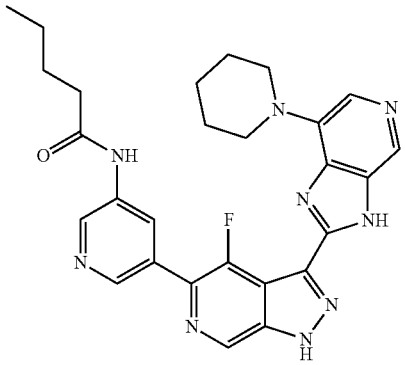
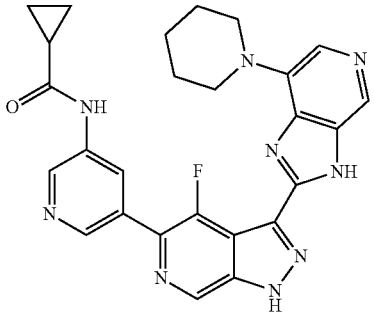
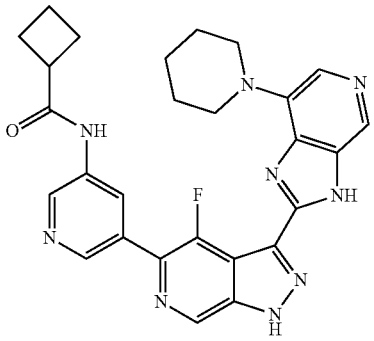
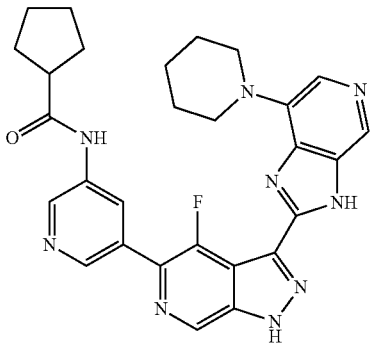
616	
617	
618	
619	

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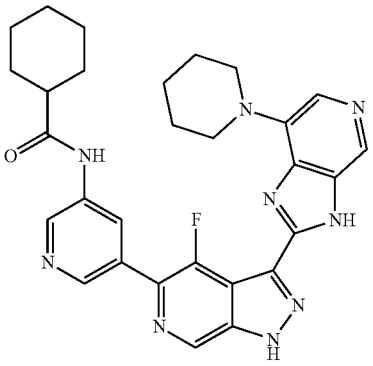
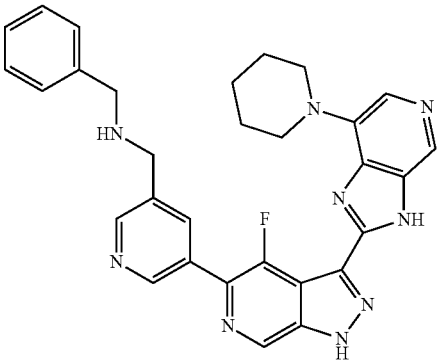
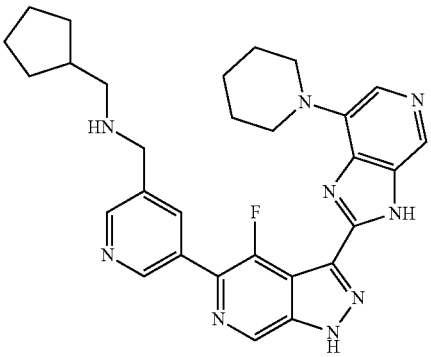
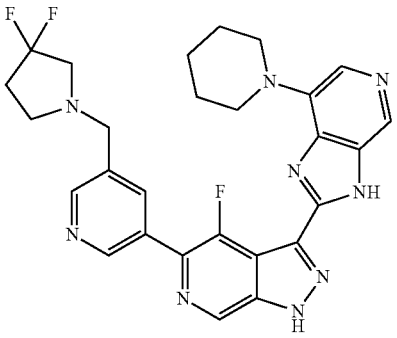
620	
621	
622	
623	

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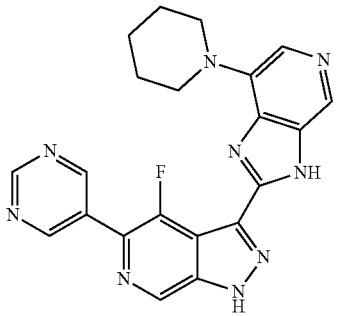

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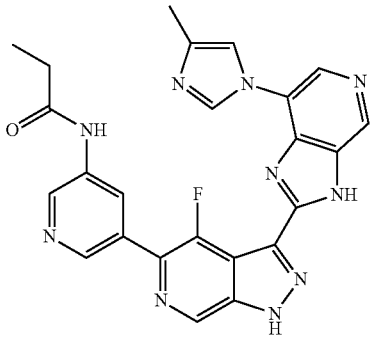

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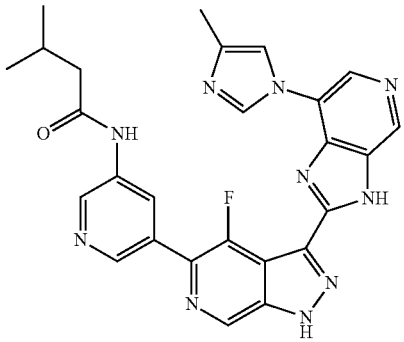

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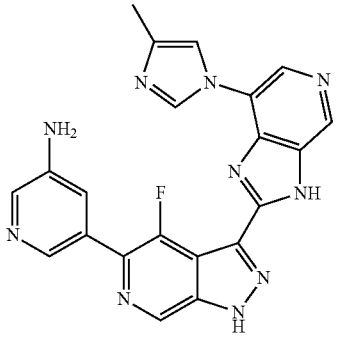

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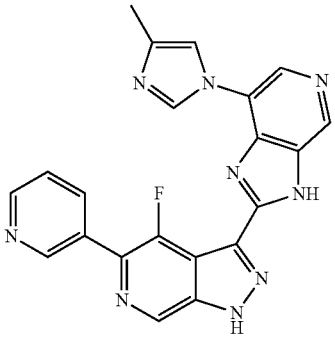

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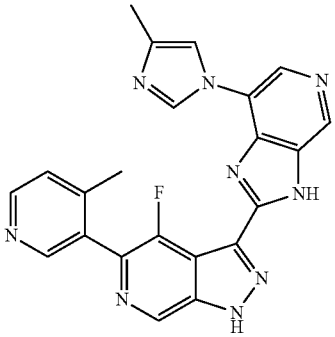

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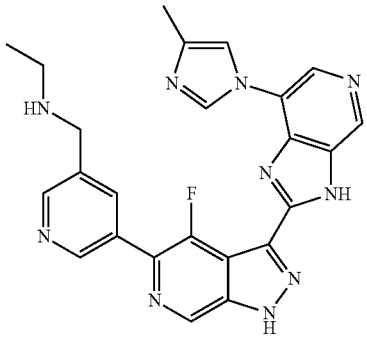

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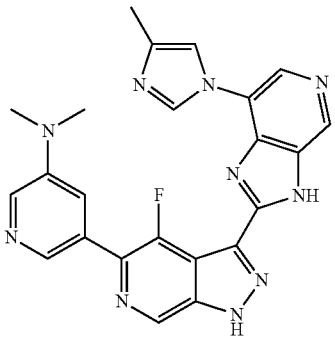

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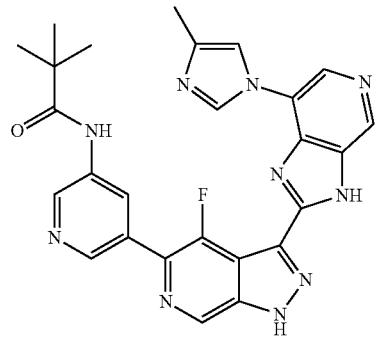
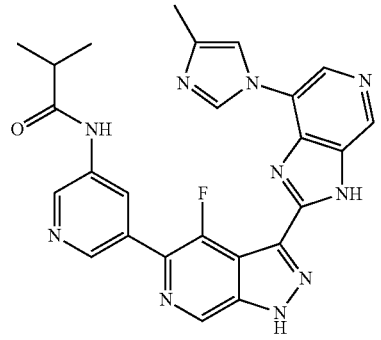
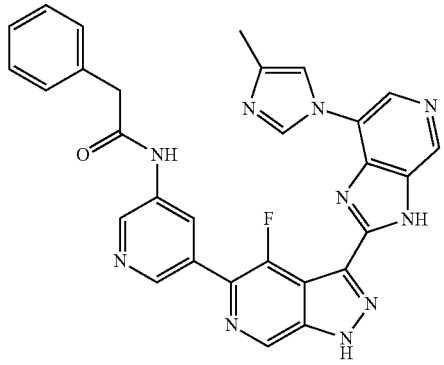
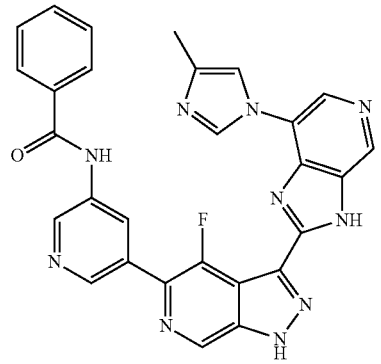
632	
633	
634	
635	

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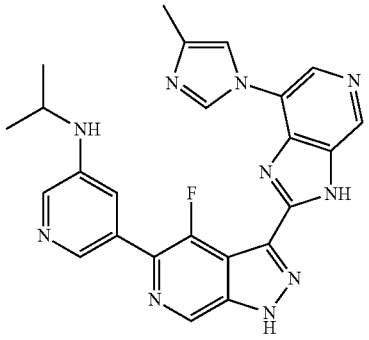
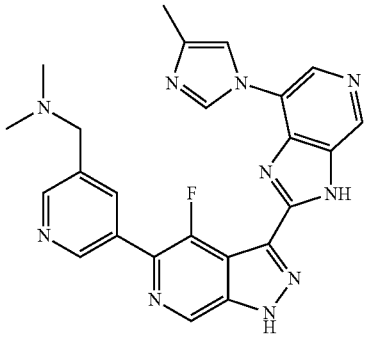
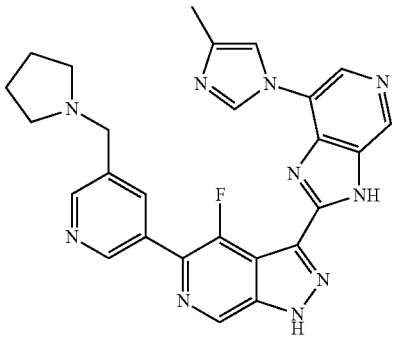
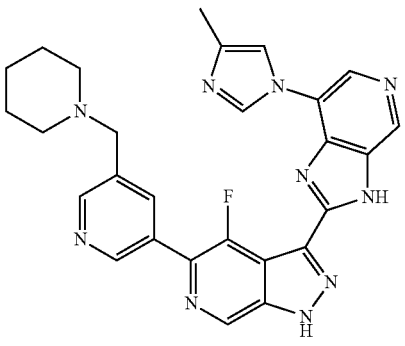
636	
637	
638	
639	

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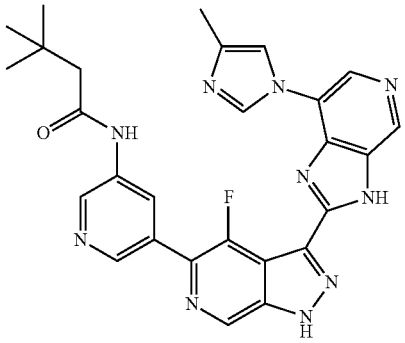
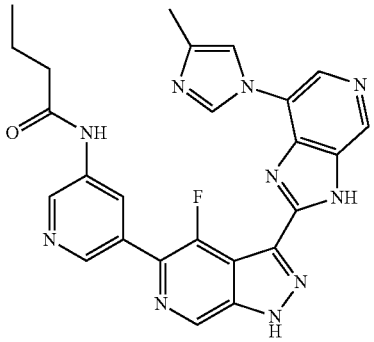
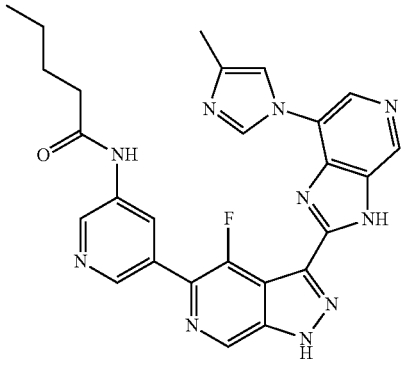
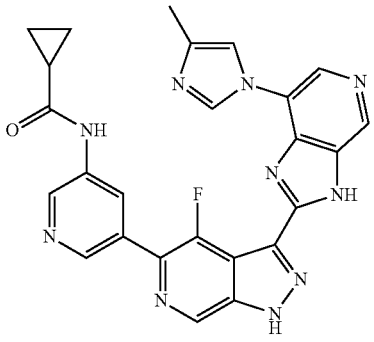
640	
641	
642	
643	

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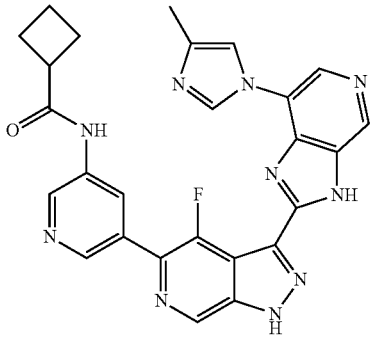
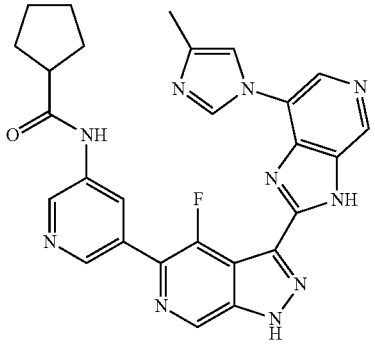
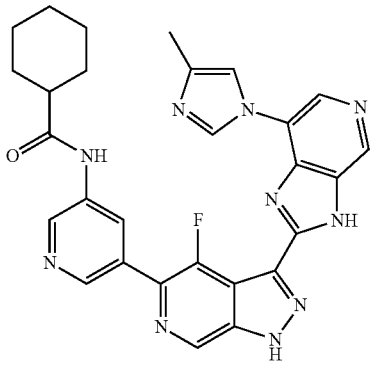
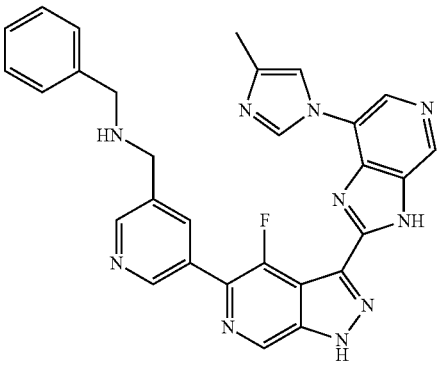
644	
645	
646	
647	

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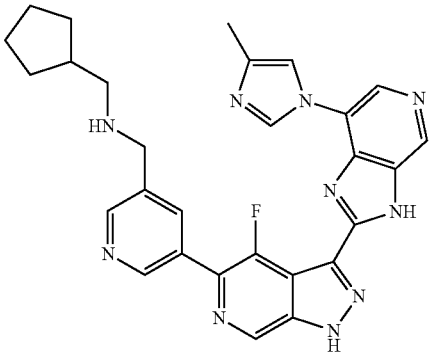
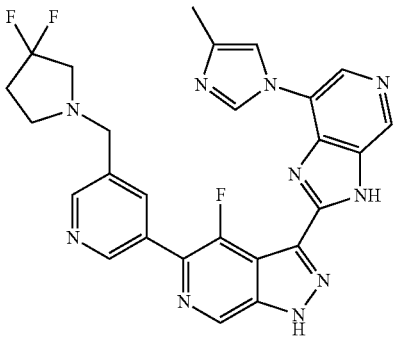
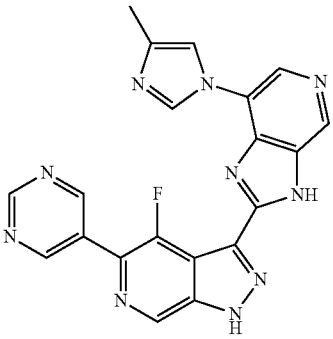
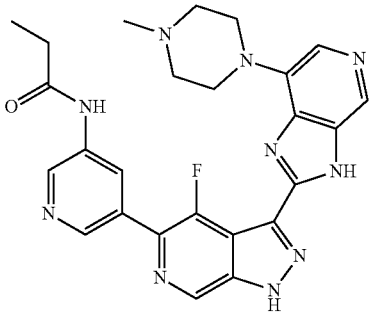
648	
649	
650	
651	

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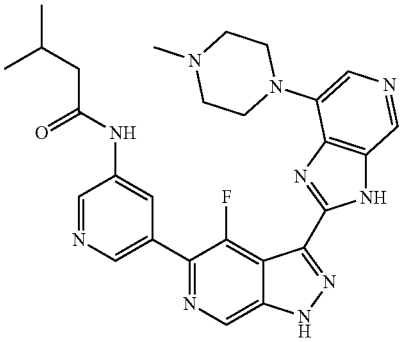
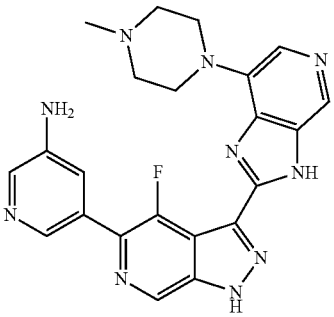
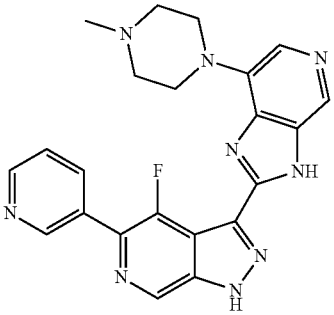
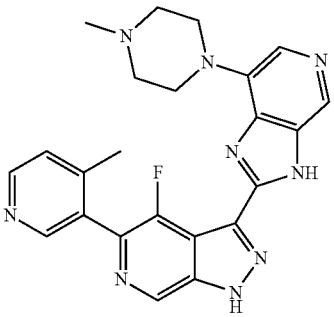
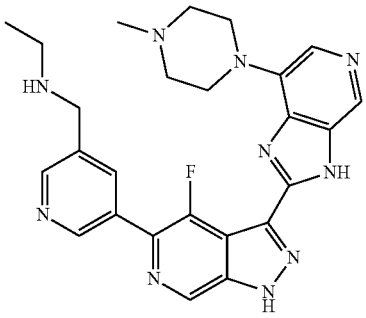
652	
653	
654	
655	
656	

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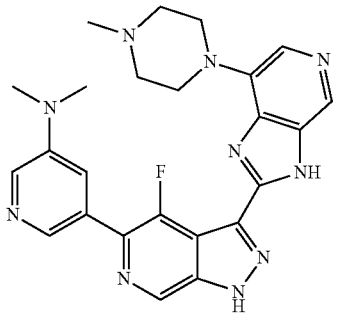
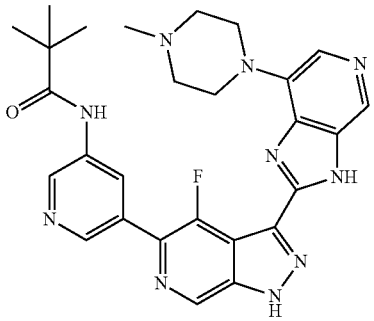
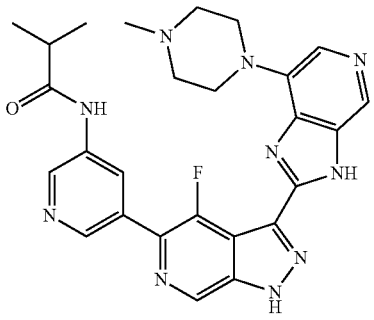
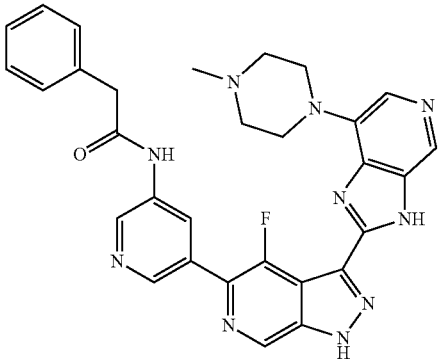
657	
658	
659	
660	

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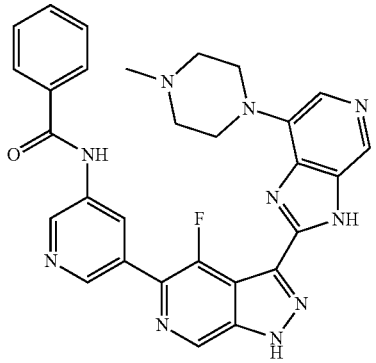
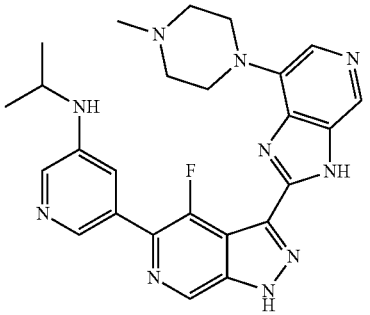
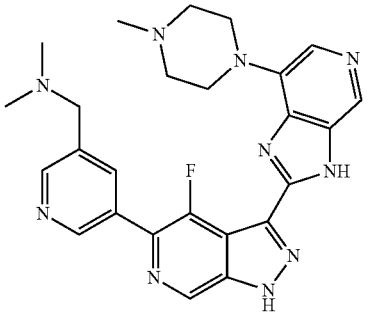
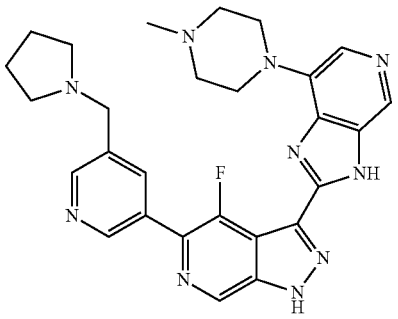
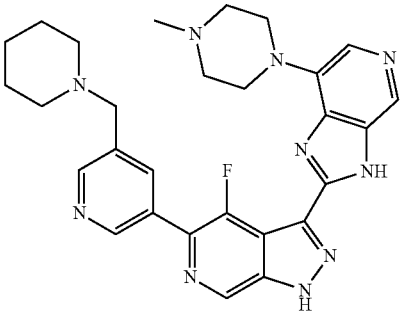
661	
662	
663	
664	
665	

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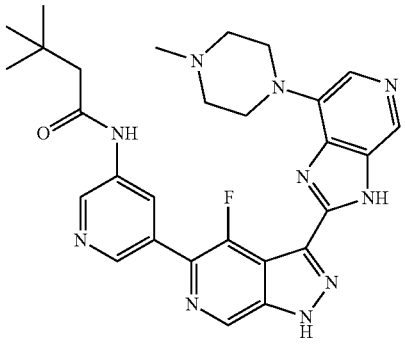
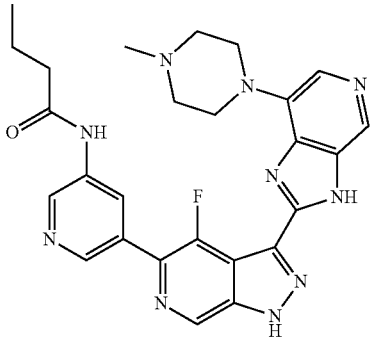
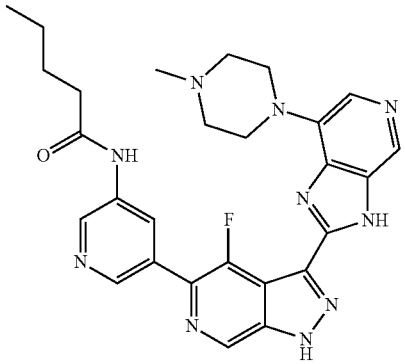
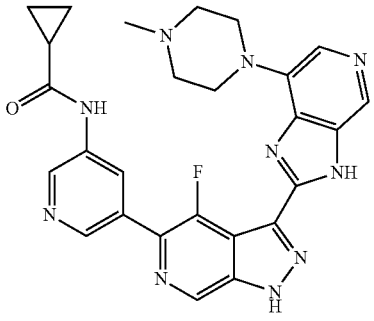
666	
667	
668	
669	

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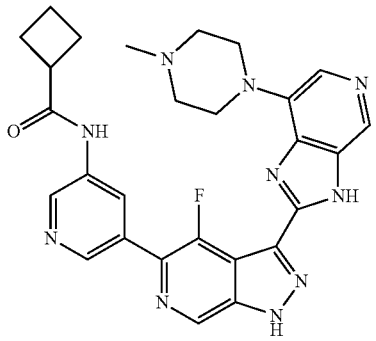
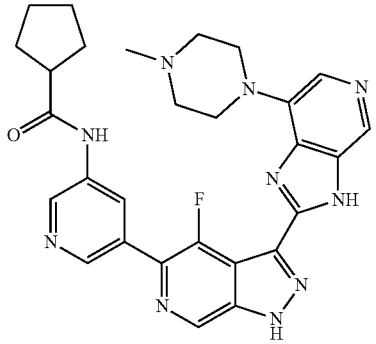
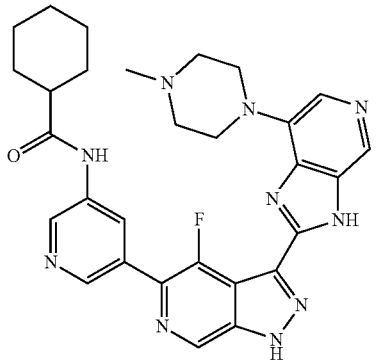
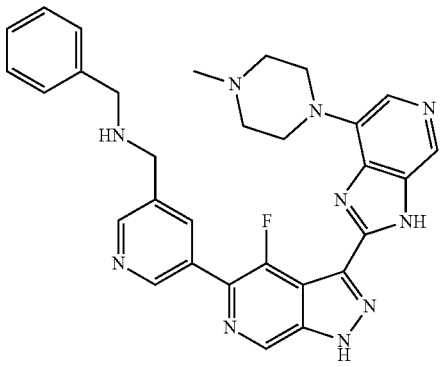
670	
671	
672	
673	

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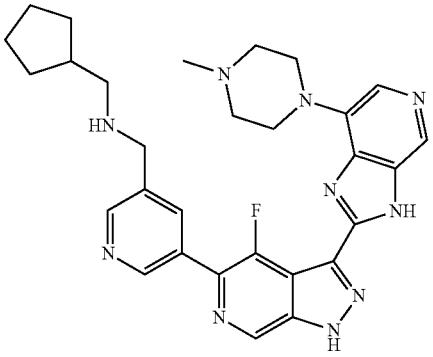
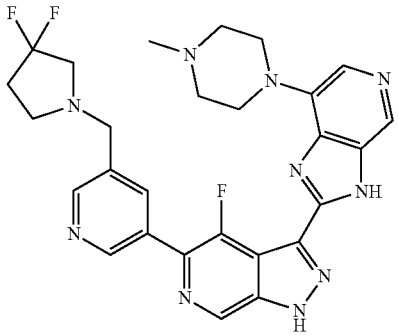
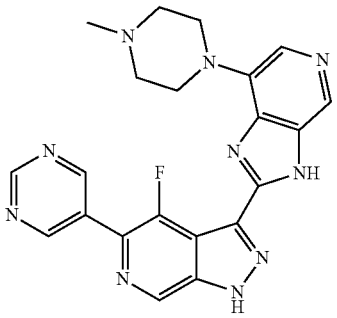
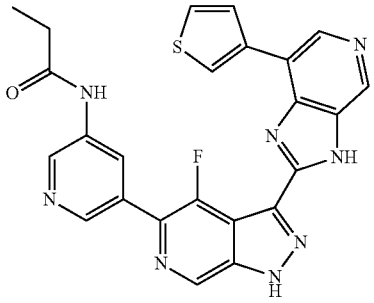
674	
675	
676	
677	

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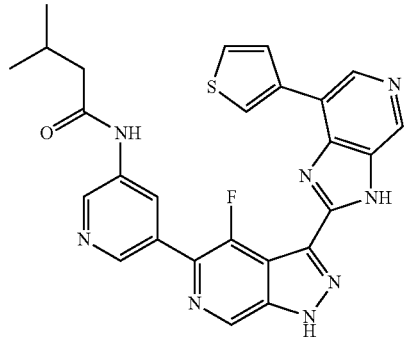
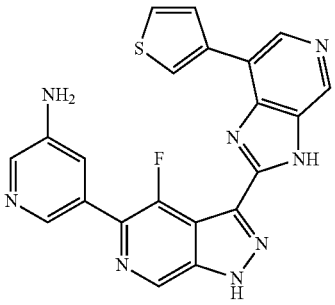
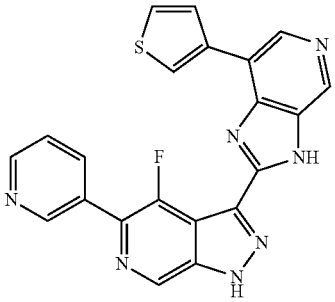
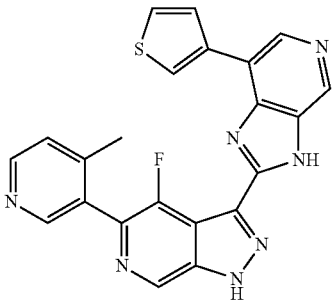
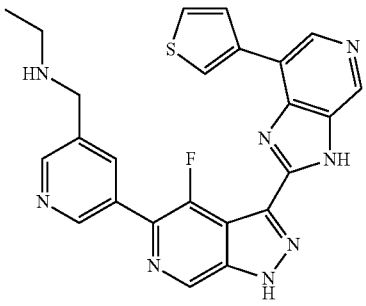
678	
679	
680	
681	
682	

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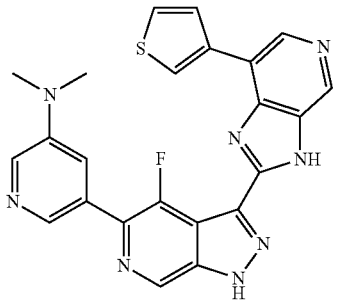
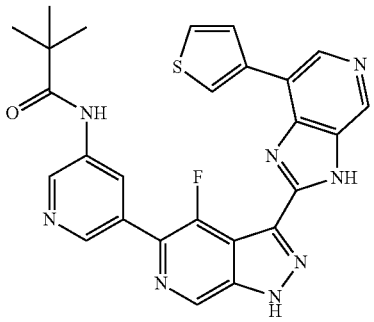
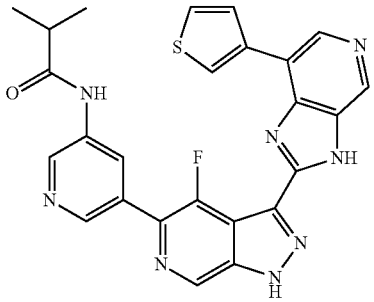
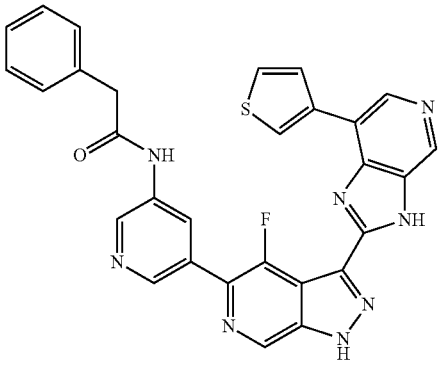
683	
684	
685	
686	

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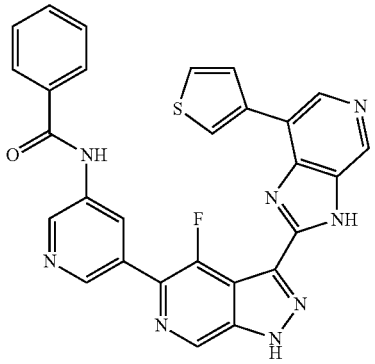
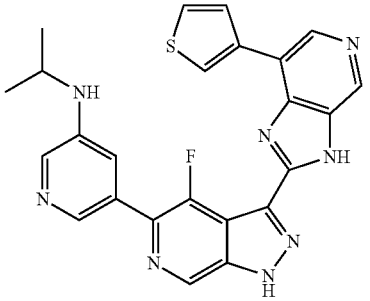
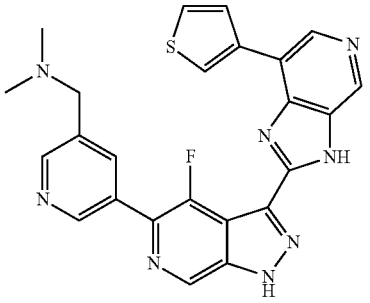
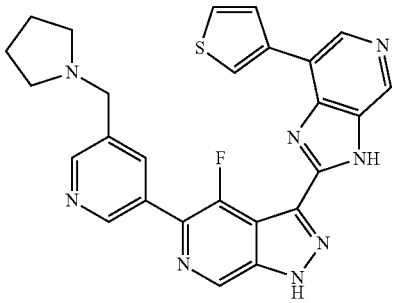
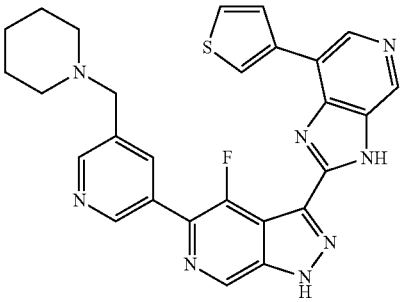
687	
688	
689	
690	
691	

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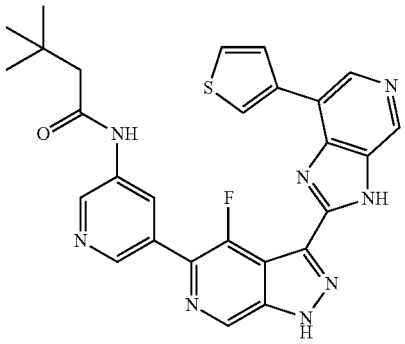
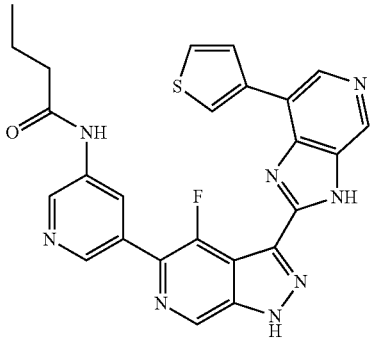
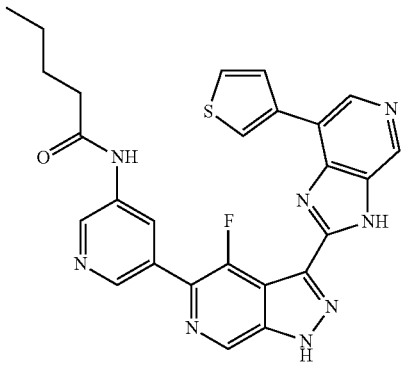
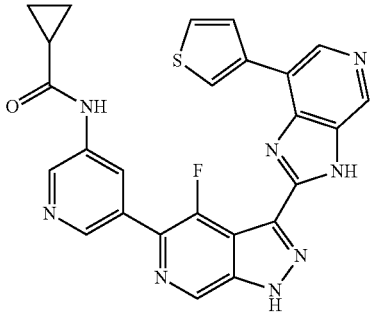
692	
693	
694	
695	

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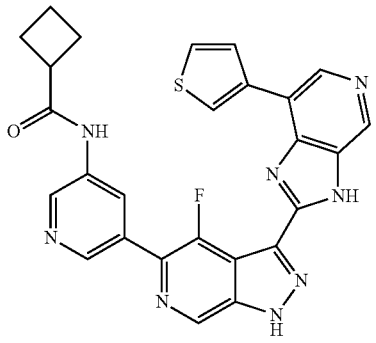
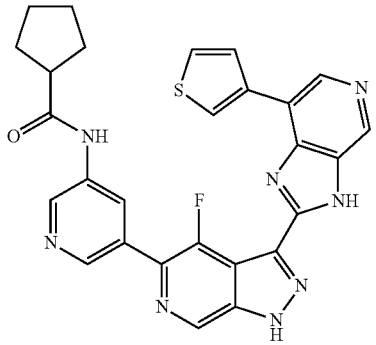
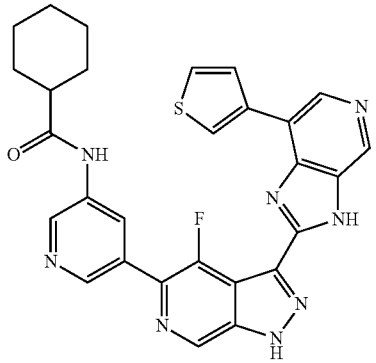
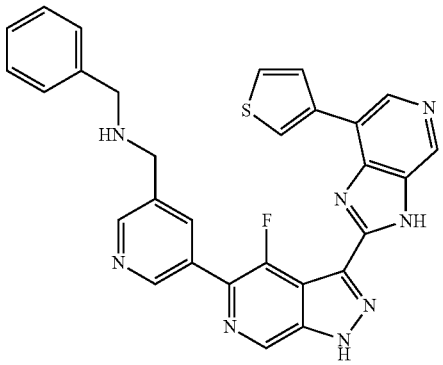
696	
697	
698	
699	

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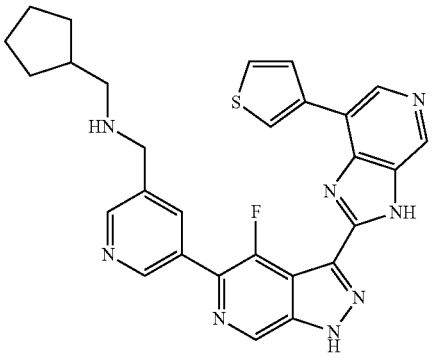
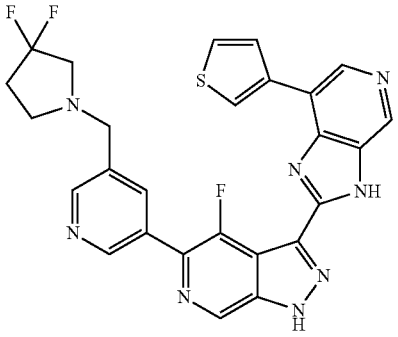
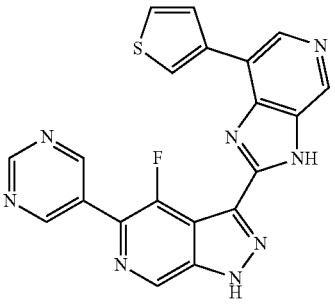
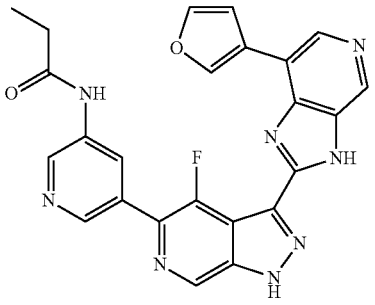
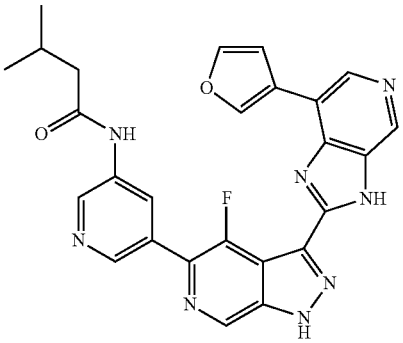
700	
701	
702	
703	
704	

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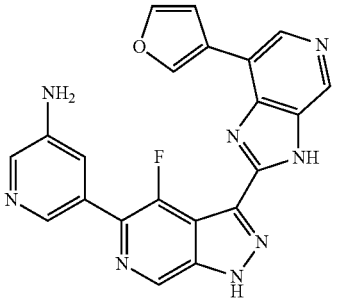
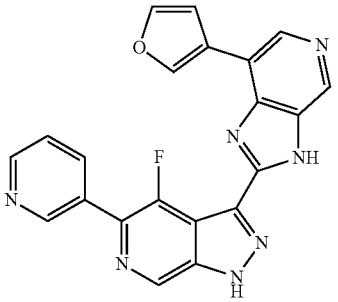
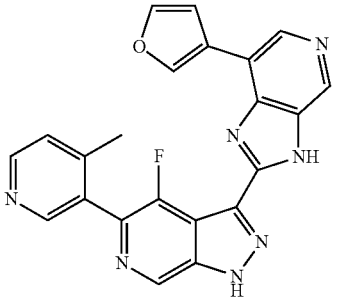
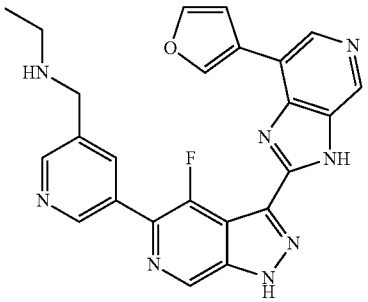
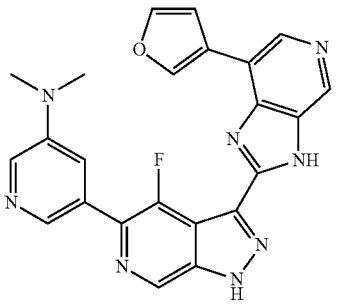
705	
706	
707	
708	
709	

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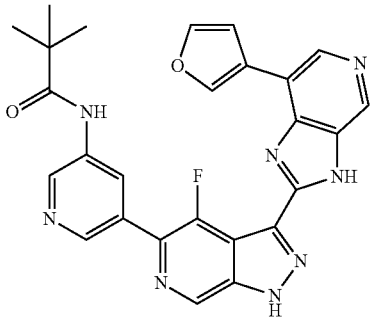
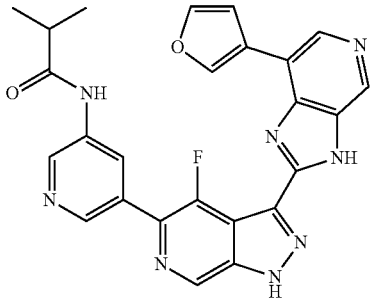
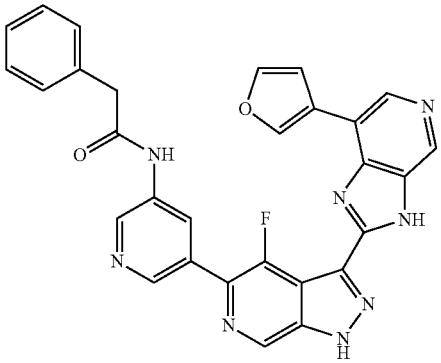
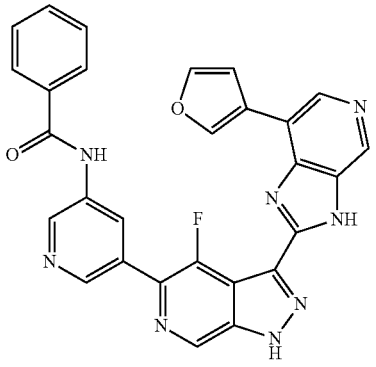
710	
711	
712	
713	

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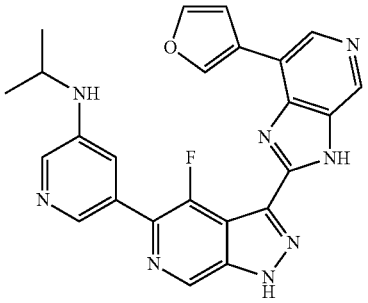
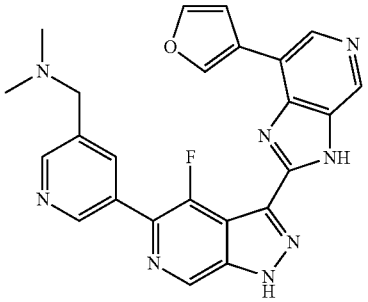
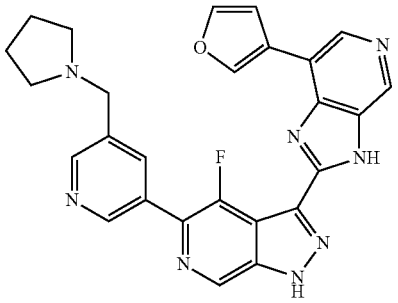
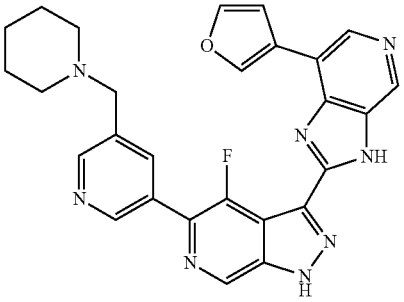
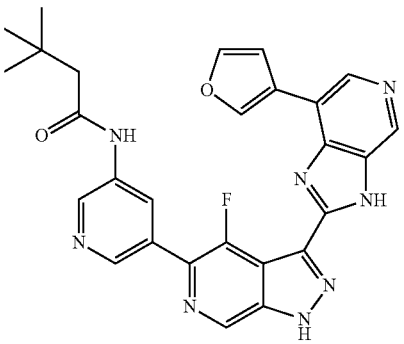
714	
715	
716	
717	
718	

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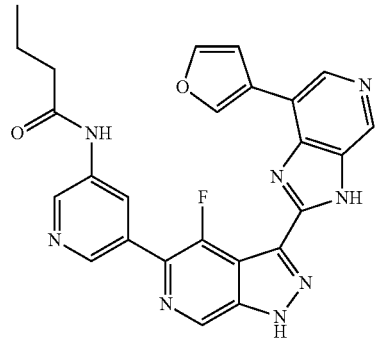
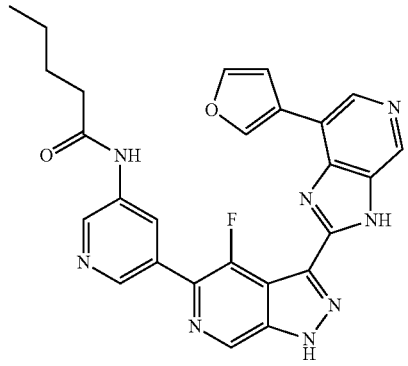
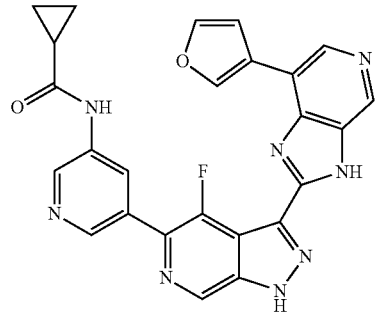
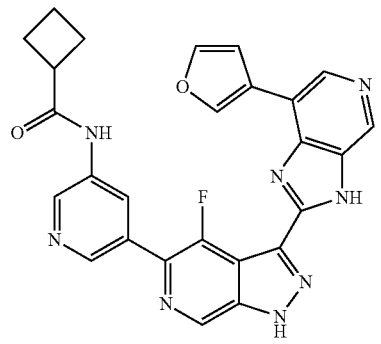
719	
720	
721	
722	

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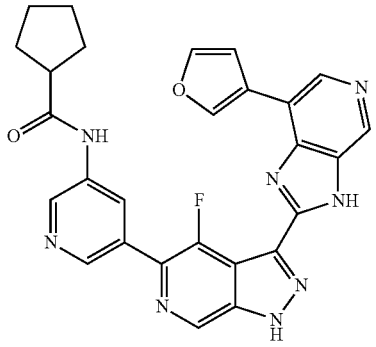
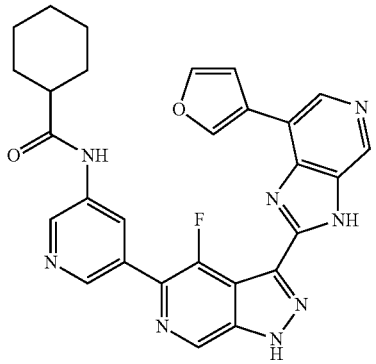
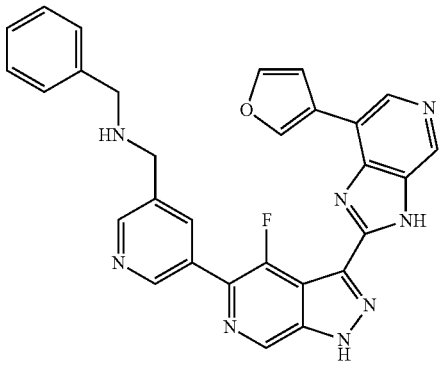
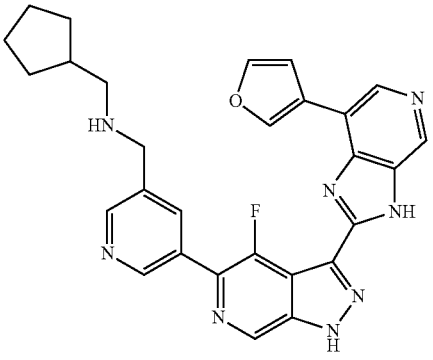
723	
724	
725	
726	

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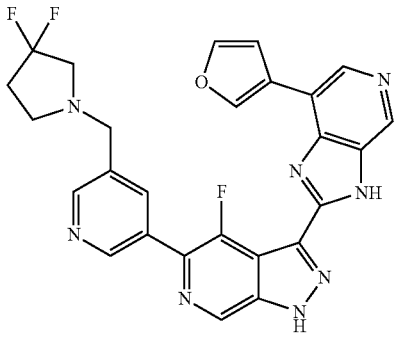
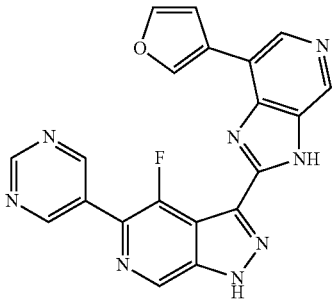
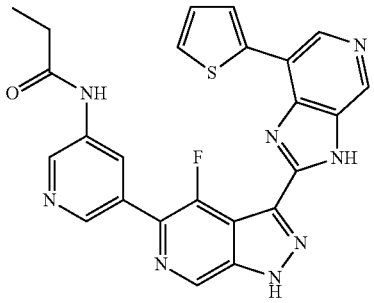
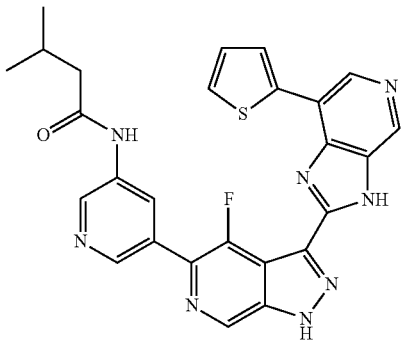
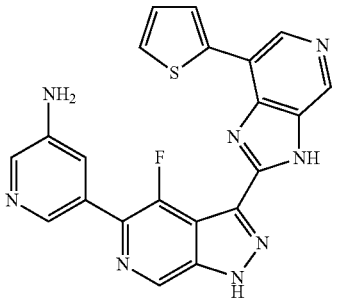
727	
728	
729	
730	
731	

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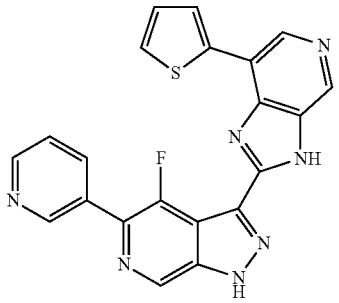
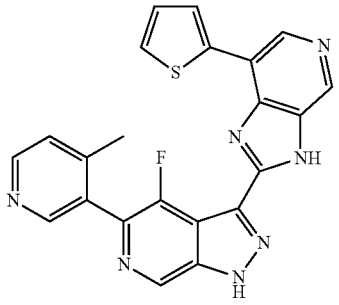
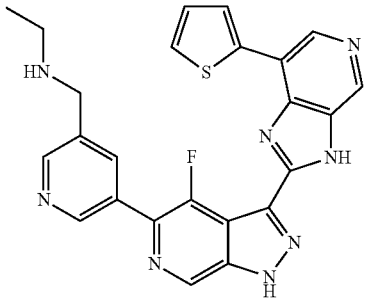
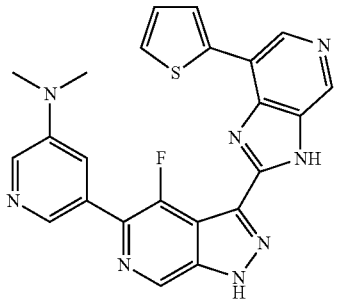
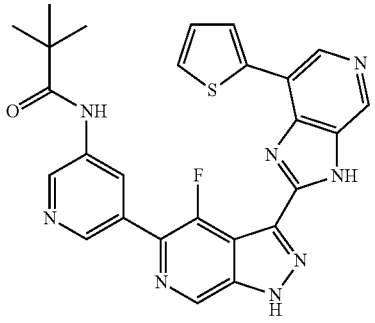
732	
733	
734	
735	
736	

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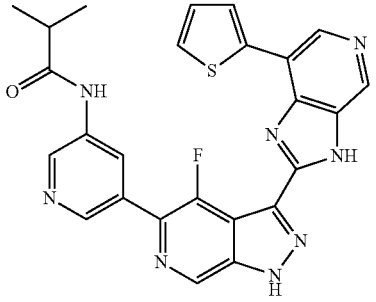
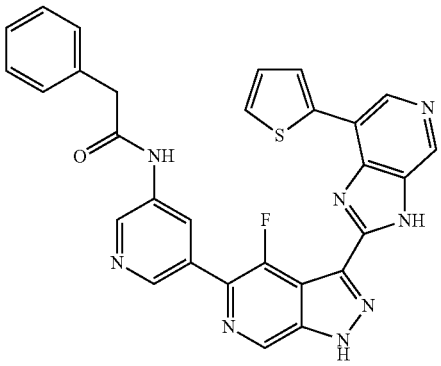
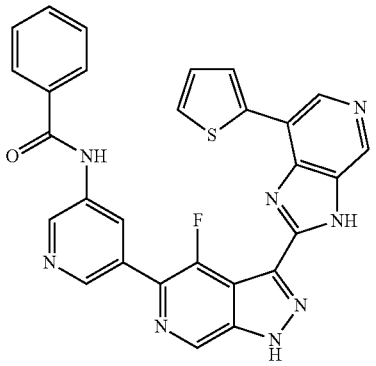
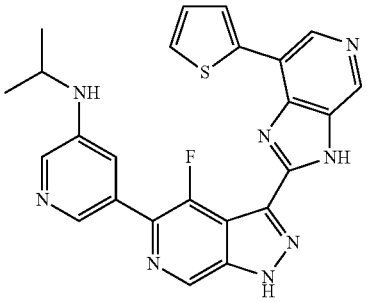
737	
738	
739	
740	

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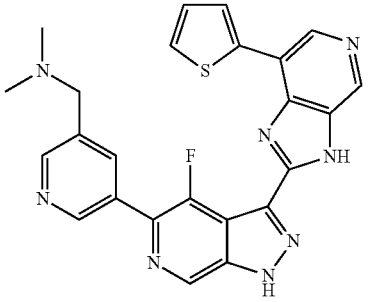
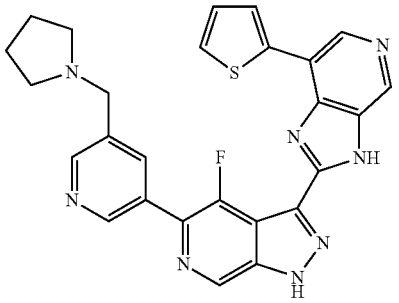
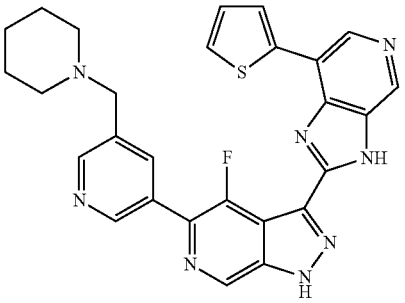
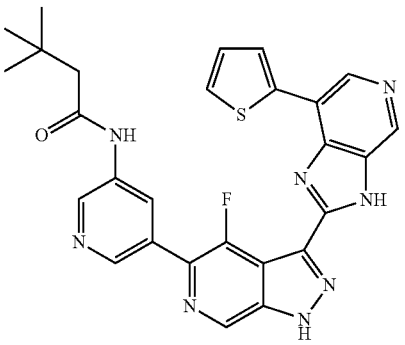
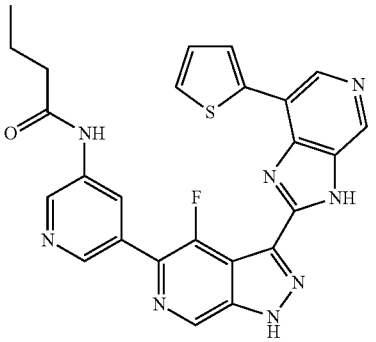
741	
742	
743	
744	
745	

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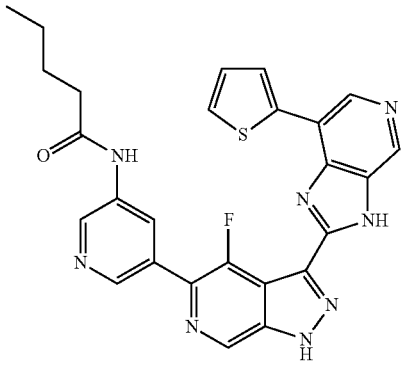
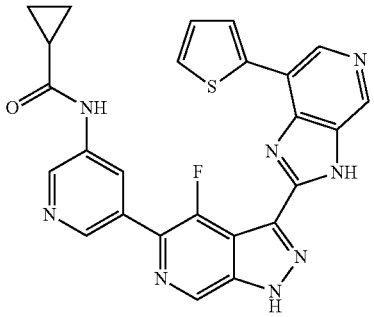
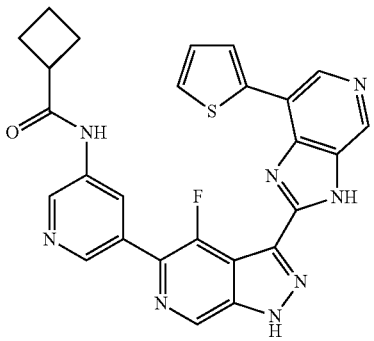
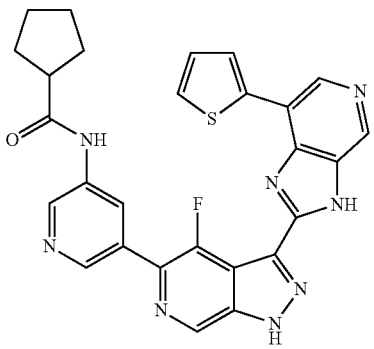
746	
747	
748	
749	

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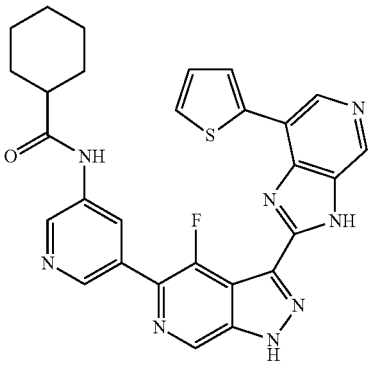
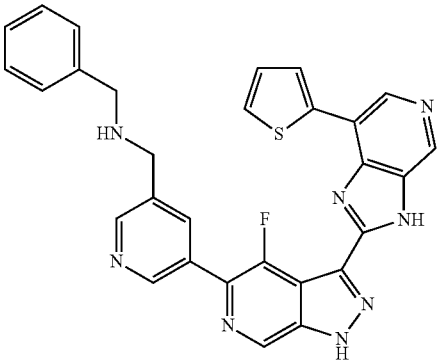
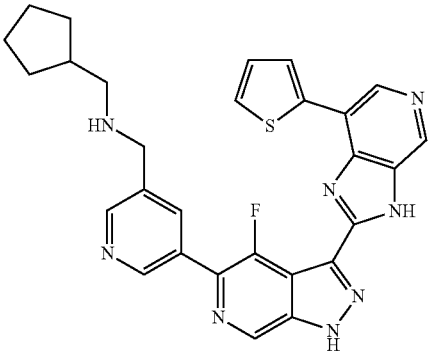
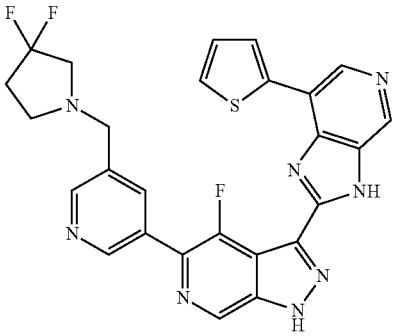
750	
751	
752	
753	

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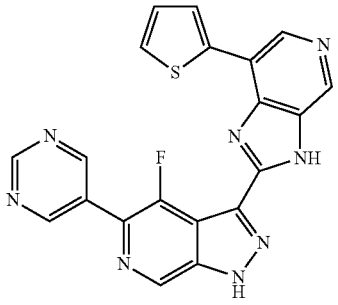
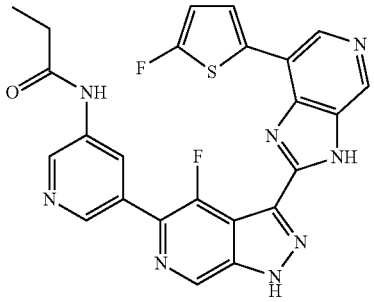
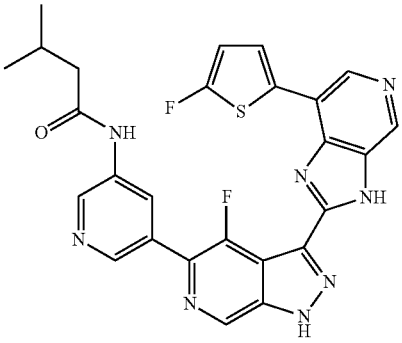
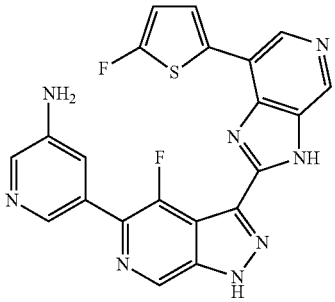
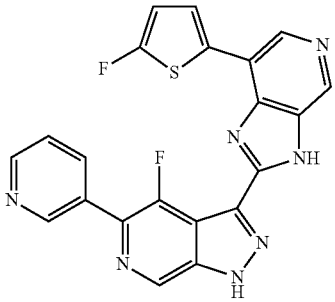
754	
755	
756	
757	
758	

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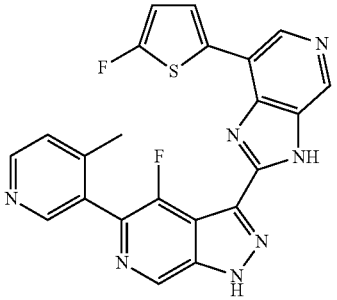
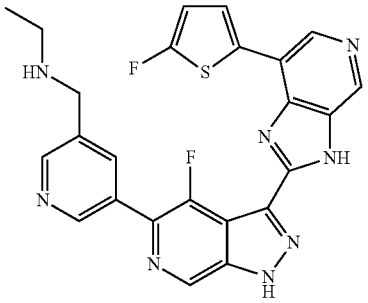
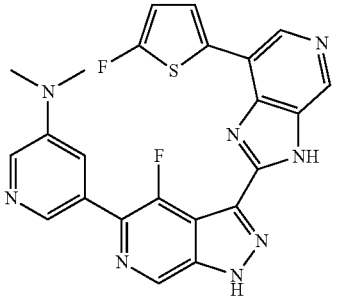
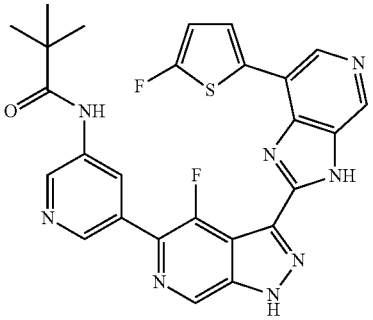
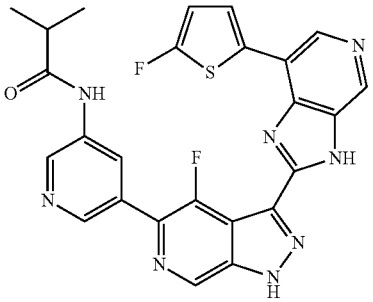
759	
760	
761	
762	
763	

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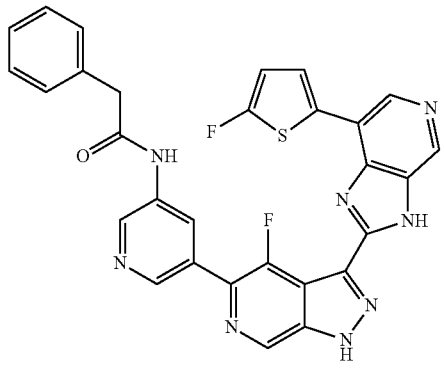
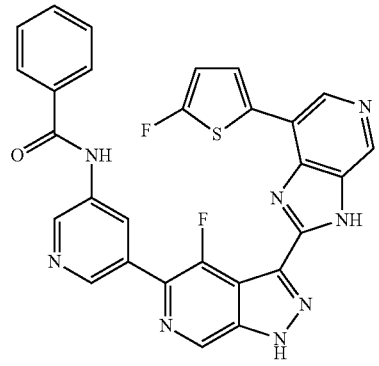
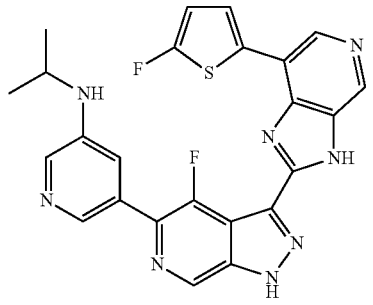
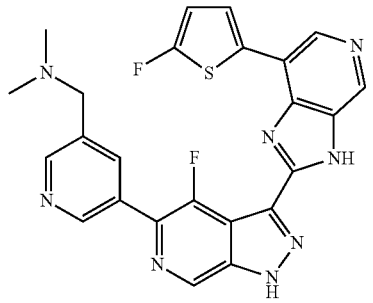
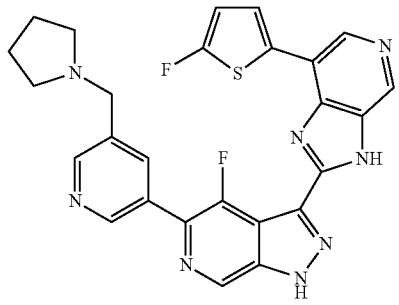
764	
765	
766	
767	
768	

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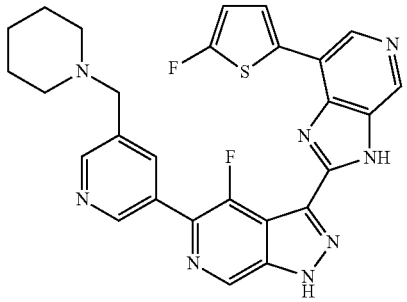
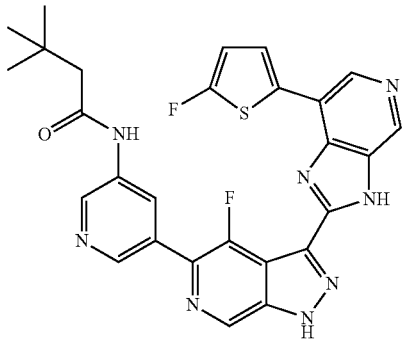
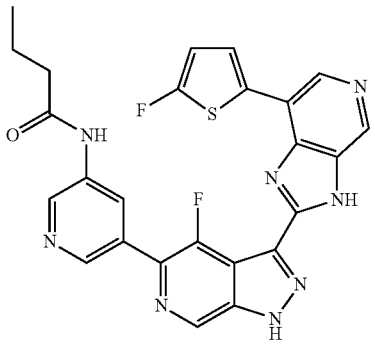
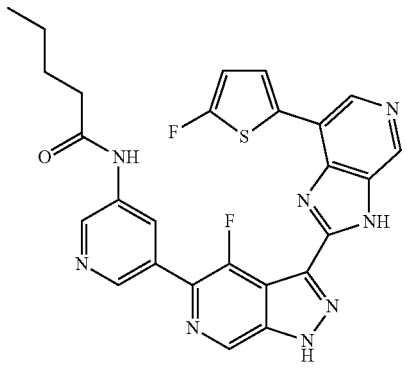
769	
770	
771	
772	

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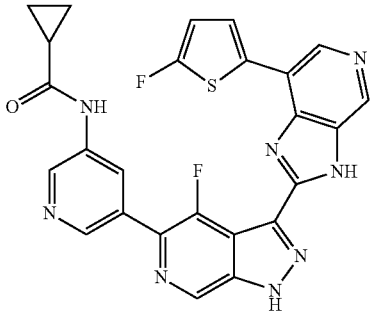
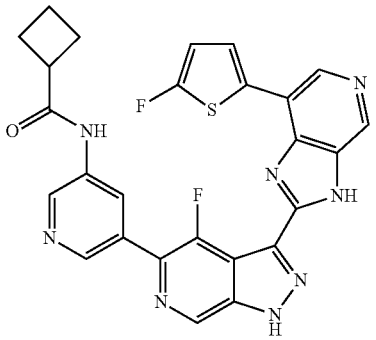
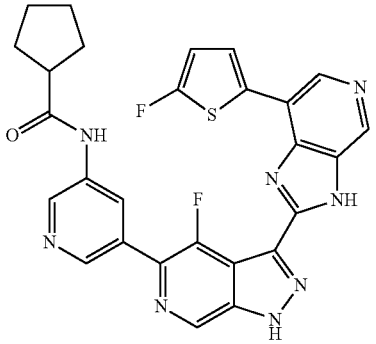
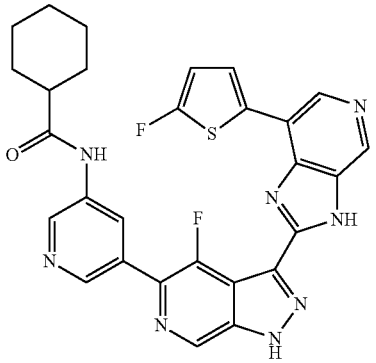
773	
774	
775	
776	

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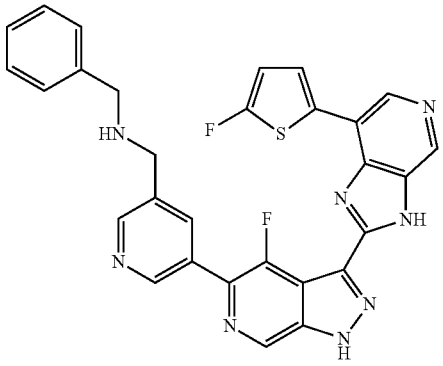
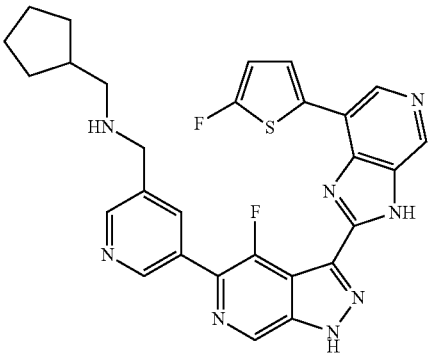
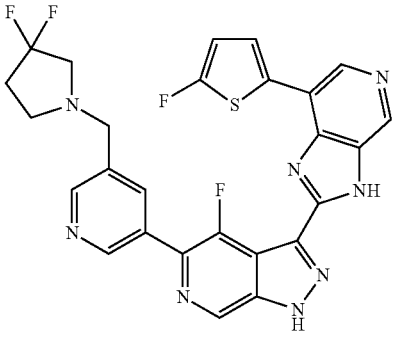
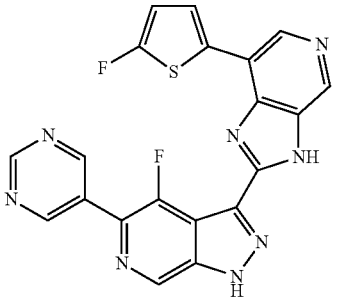
777	
778	
779	
780	

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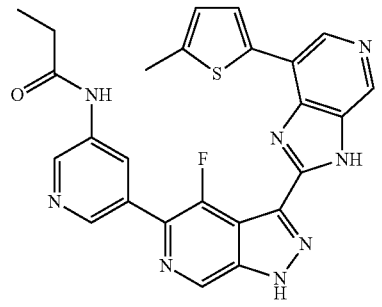
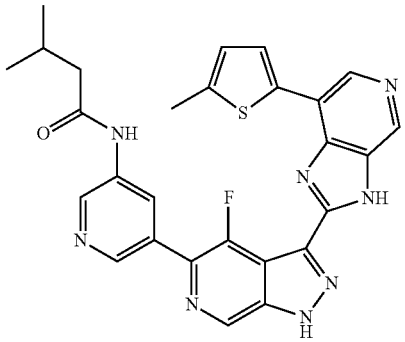
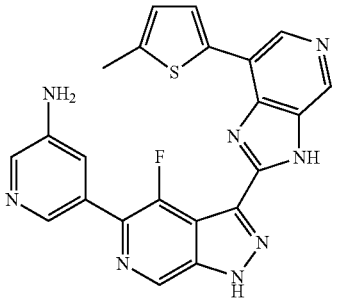
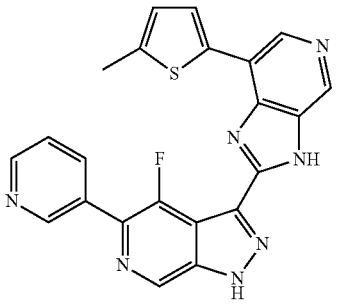
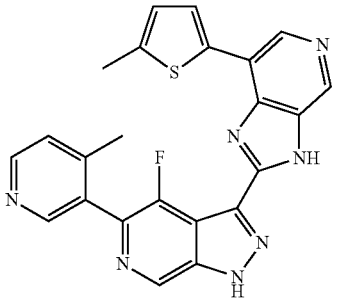
781	
782	
783	
784	
785	

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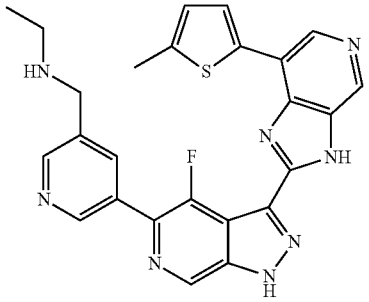
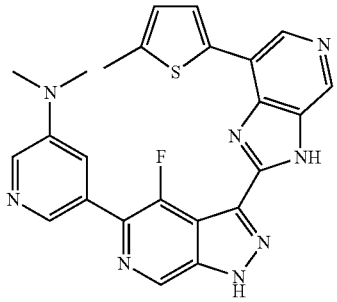
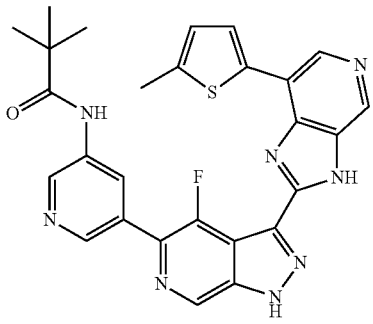
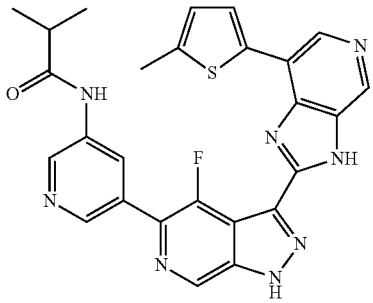
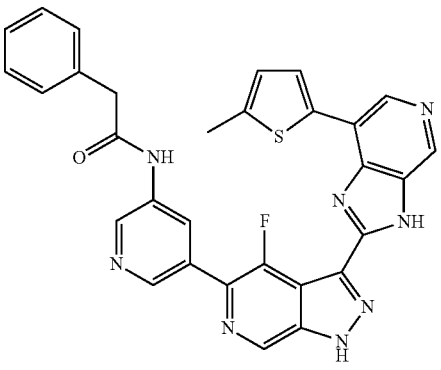
786	
787	
788	
789	
790	

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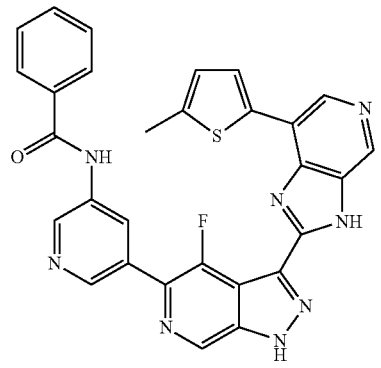
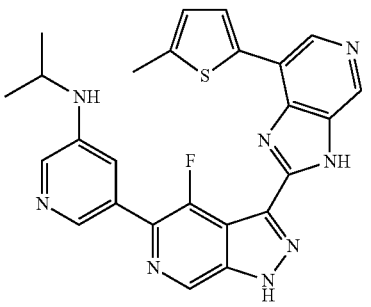
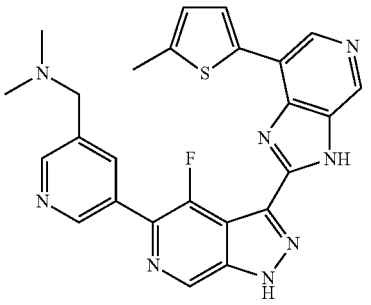
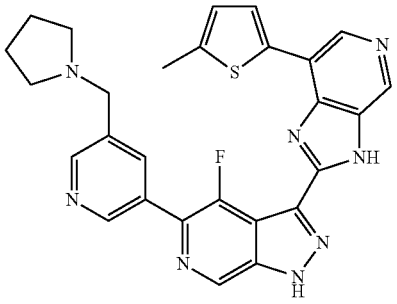
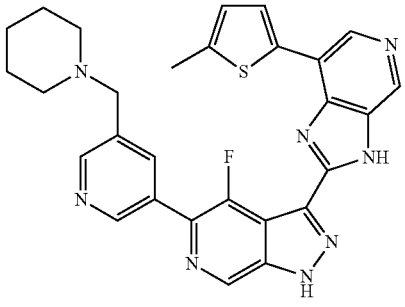
791	
792	
793	
794	
795	

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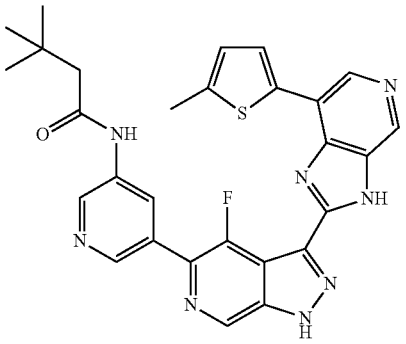
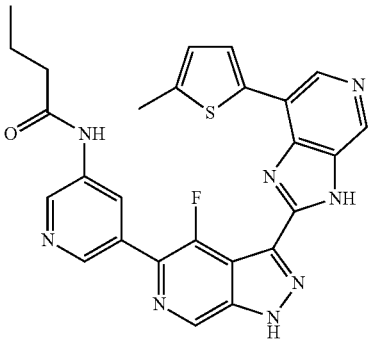
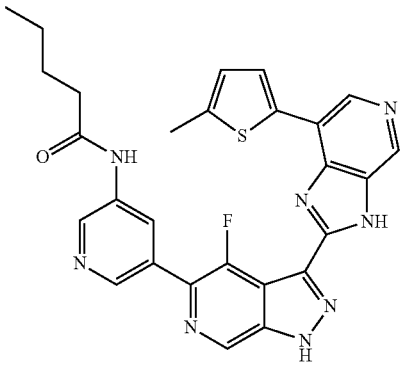
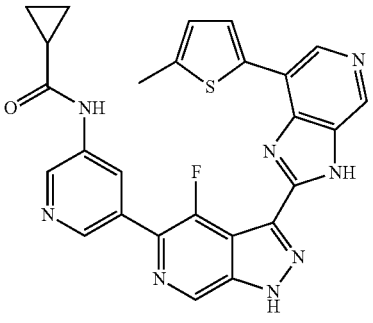
796	
797	
798	
799	

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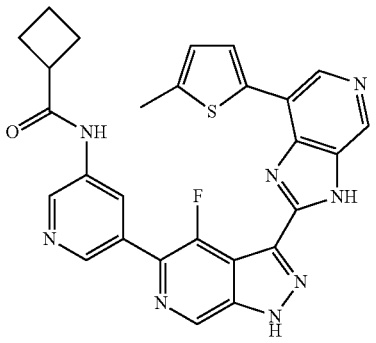
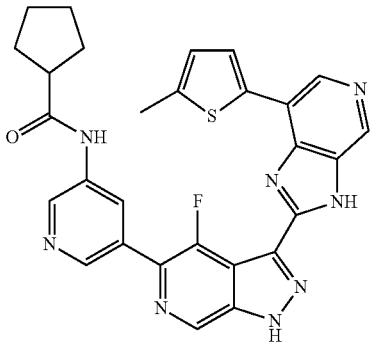
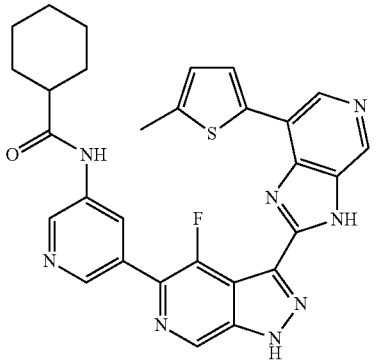
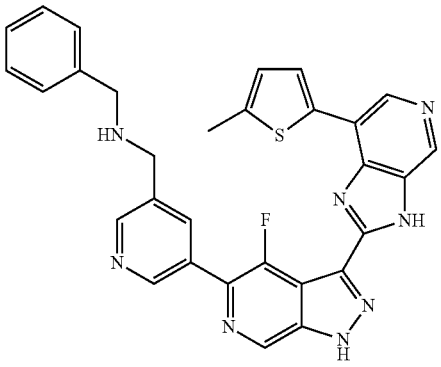
800	
801	
802	
803	

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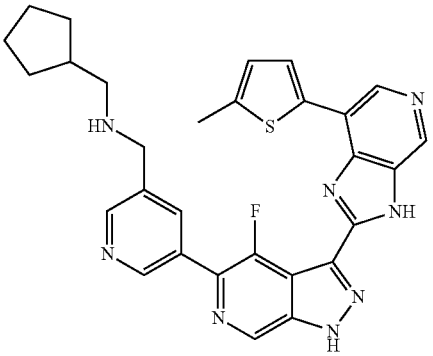
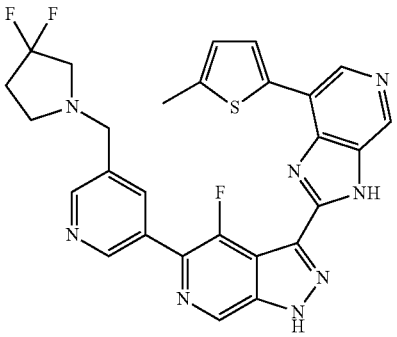
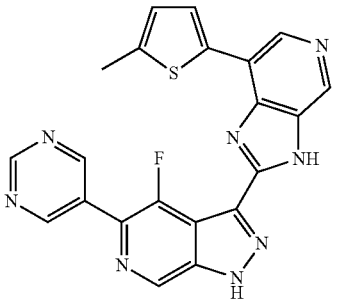
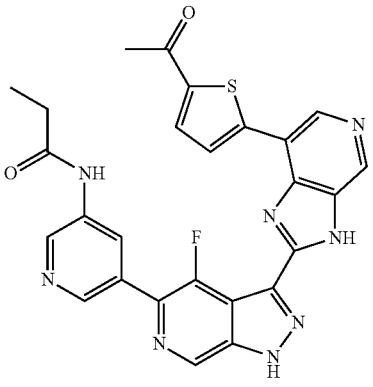
804	
805	
806	
807	

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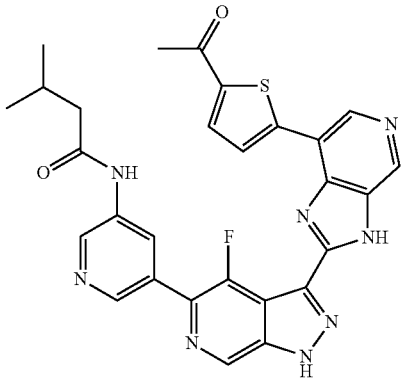
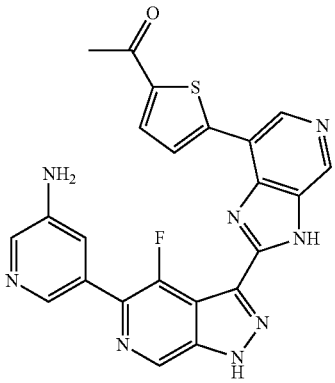
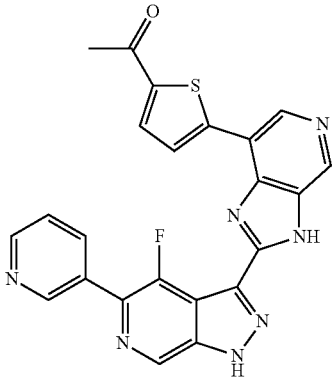
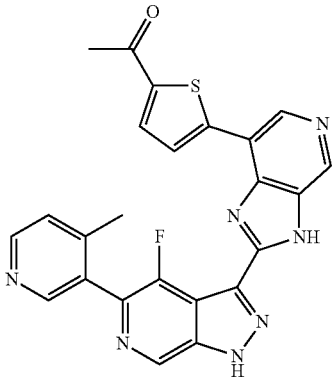
808	
809	
810	
811	

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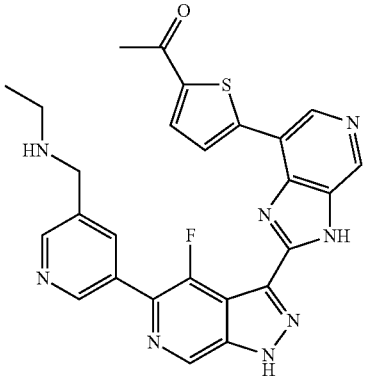
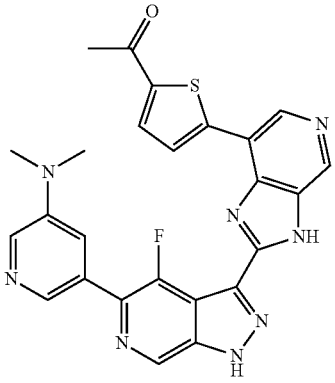
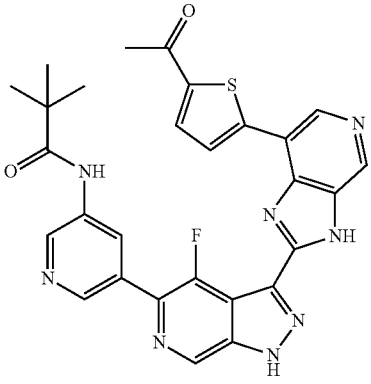
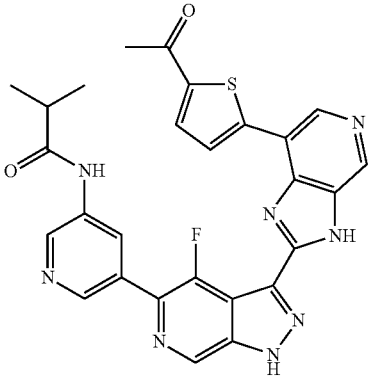
812	
813	
814	
815	

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TABLE 1-continued

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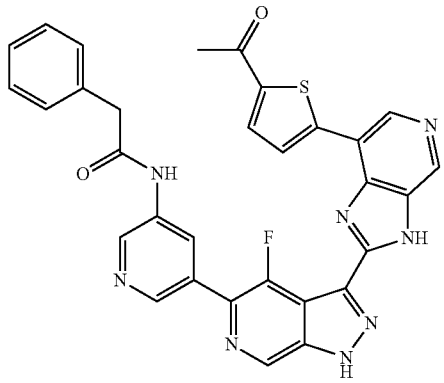

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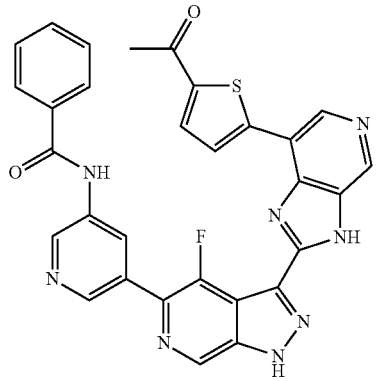

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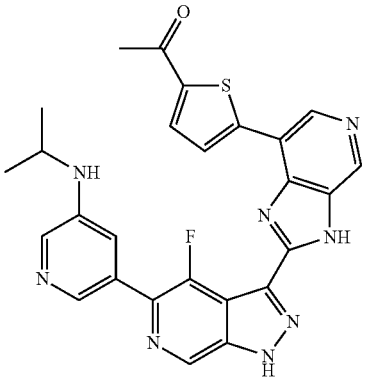

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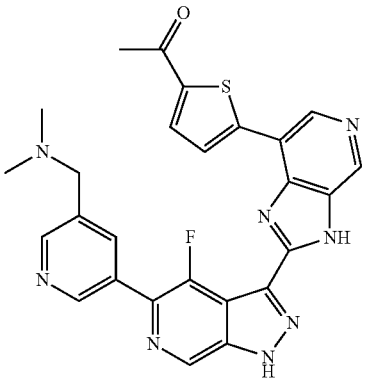

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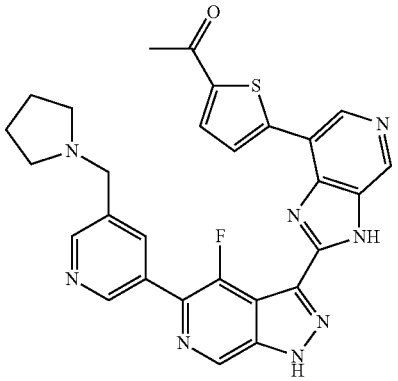

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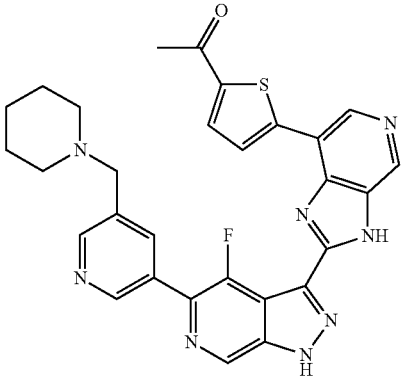

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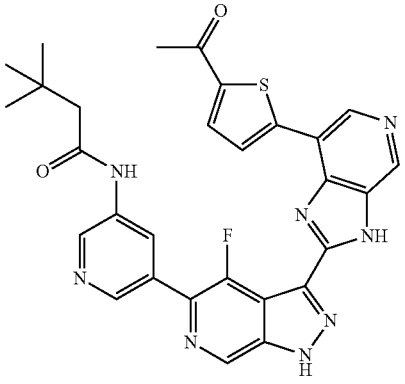

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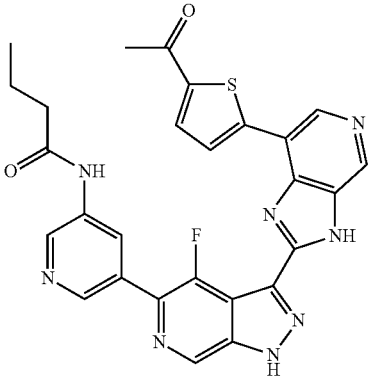

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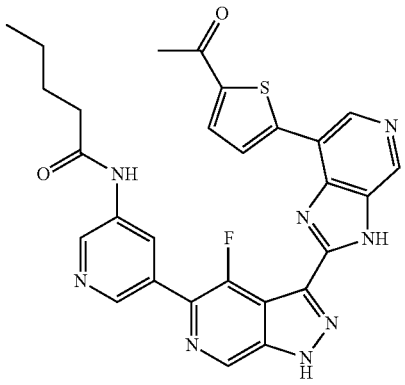

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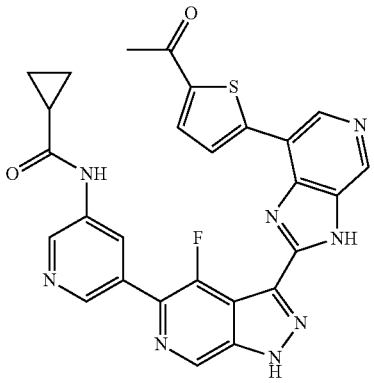

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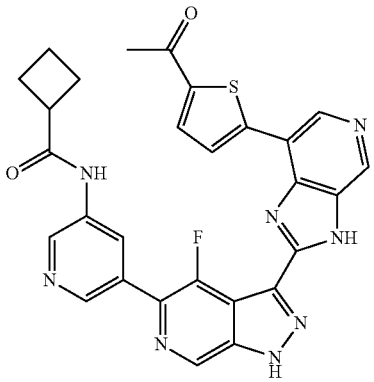

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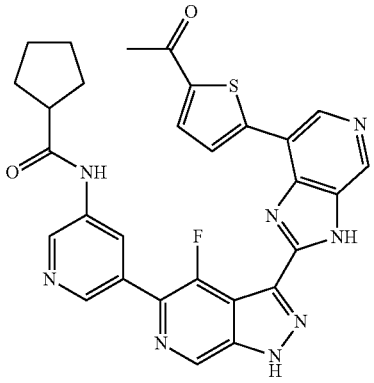

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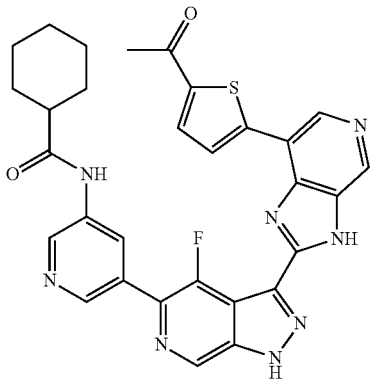

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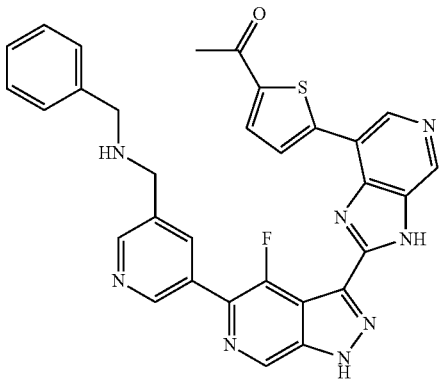

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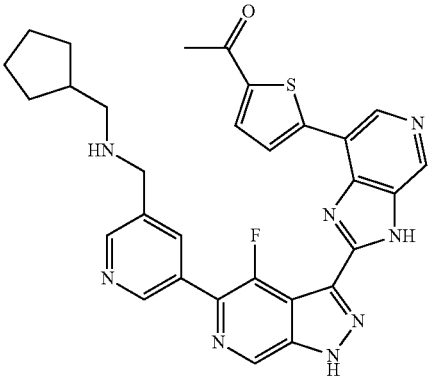

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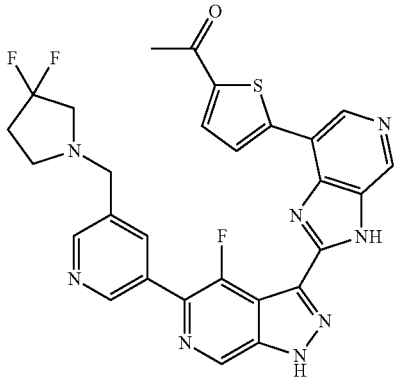

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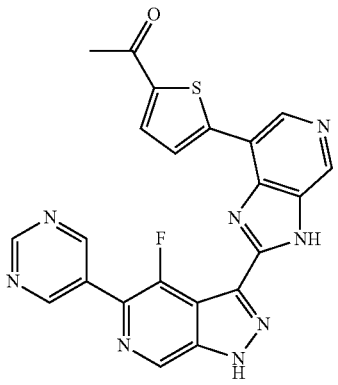
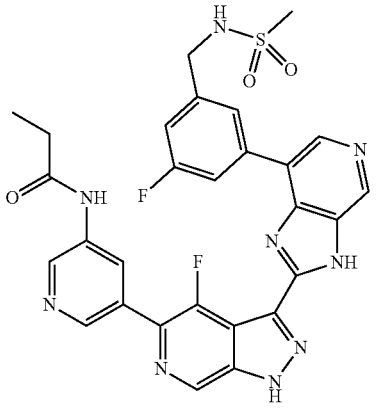
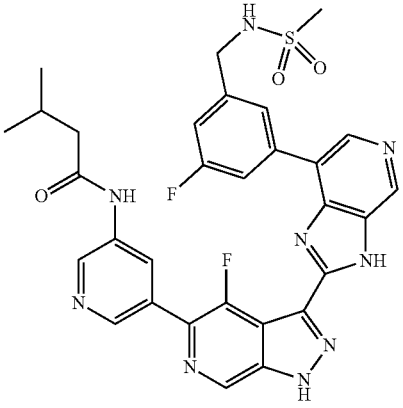
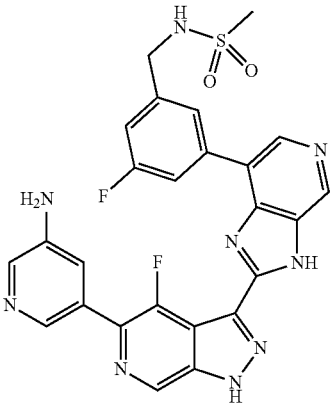
832	
833	
834	
835	

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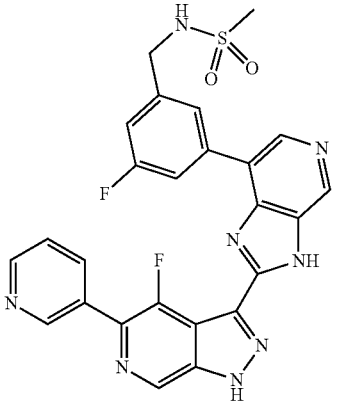
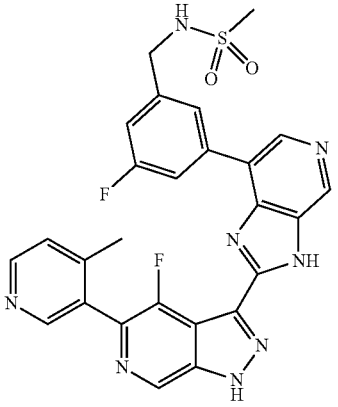
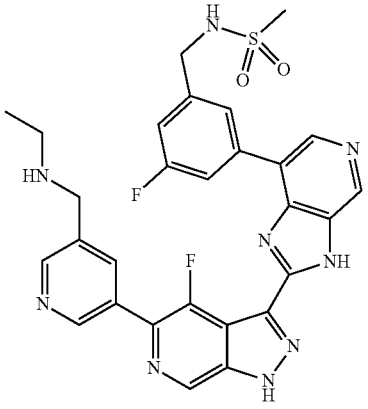
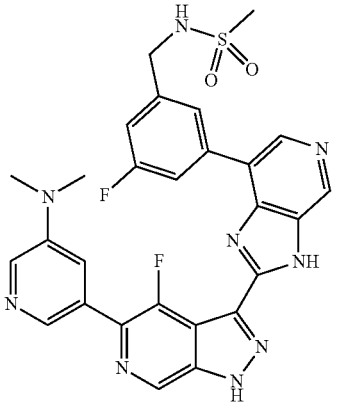
836	
837	
838	
839	

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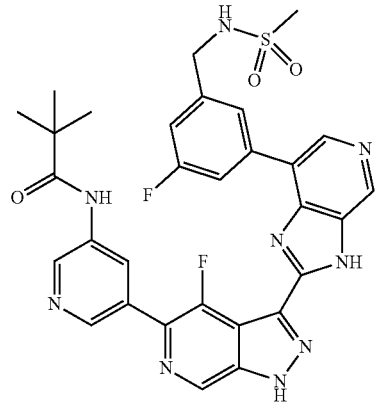
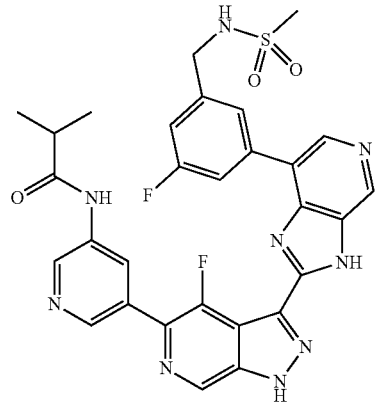
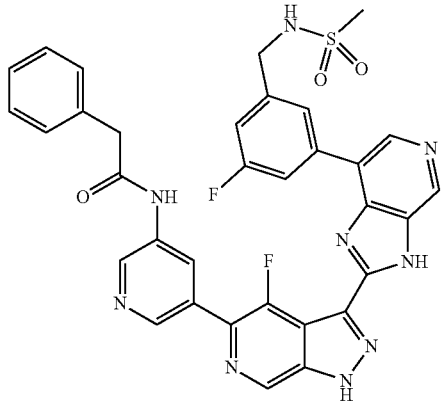
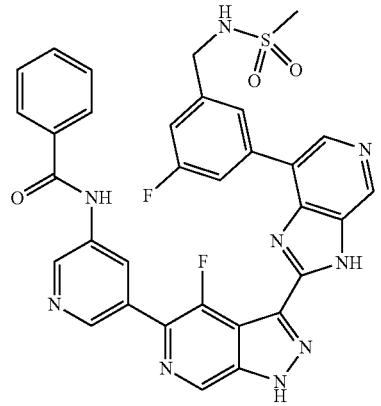
840	
841	
842	
843	

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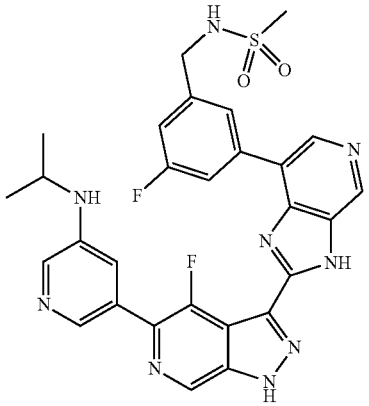
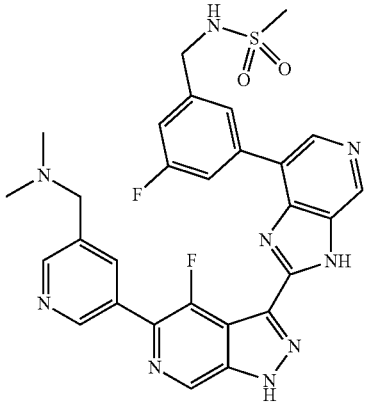
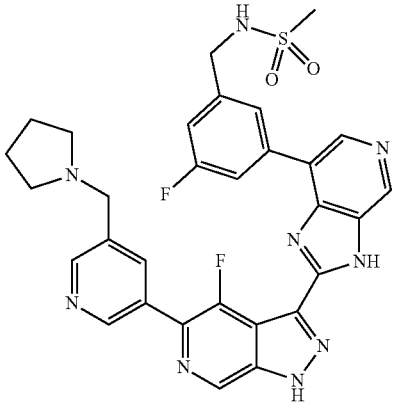
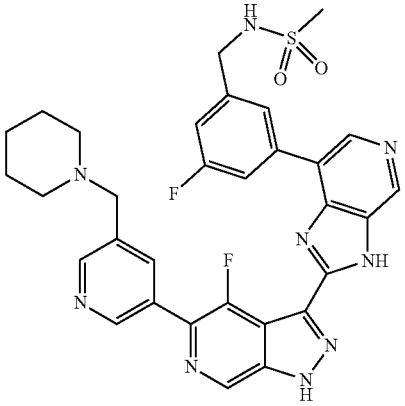
844	
845	
846	
847	

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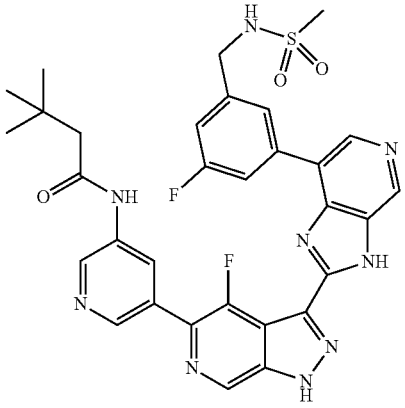
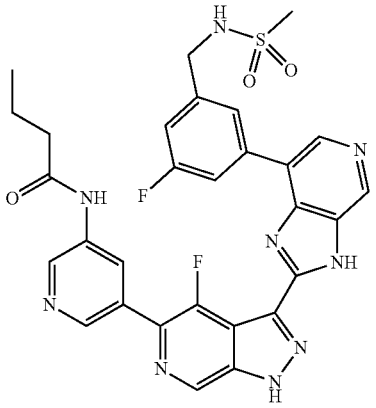
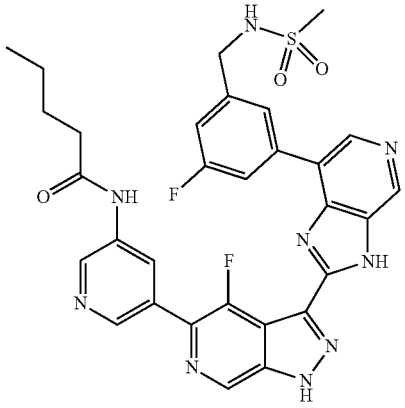
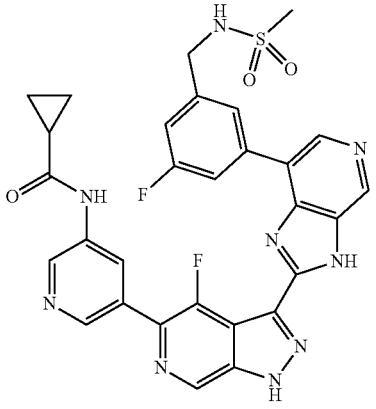
848	
849	
850	
851	

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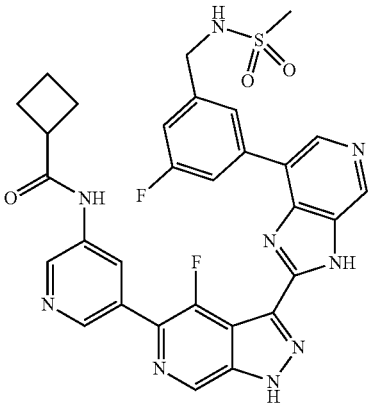
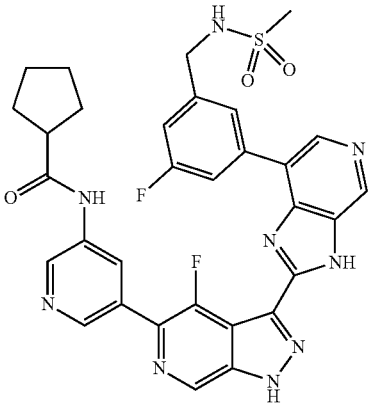
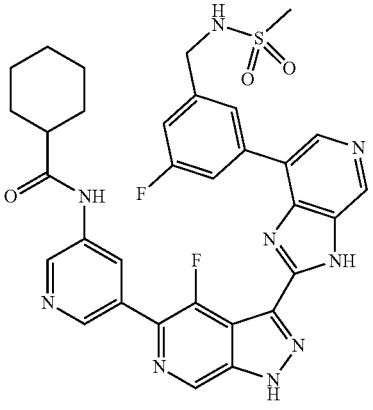
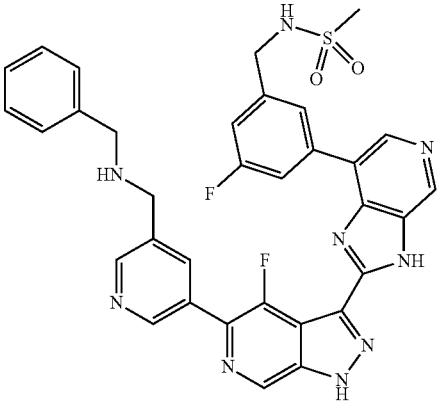
852	
853	
854	
855	

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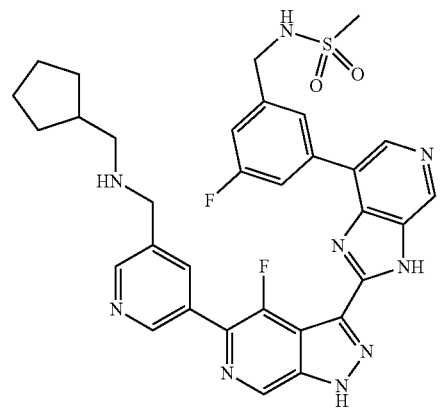
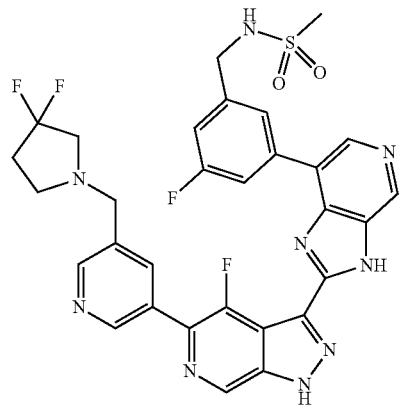
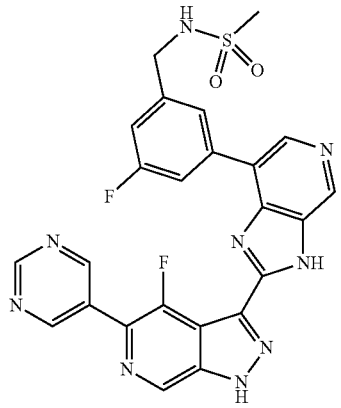
856	
857	
858	

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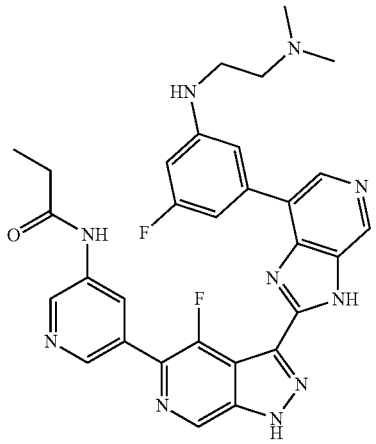
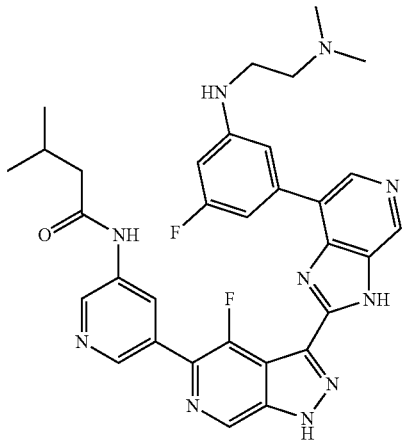
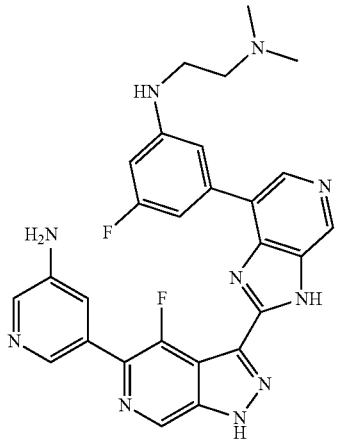
859	
860	
861	

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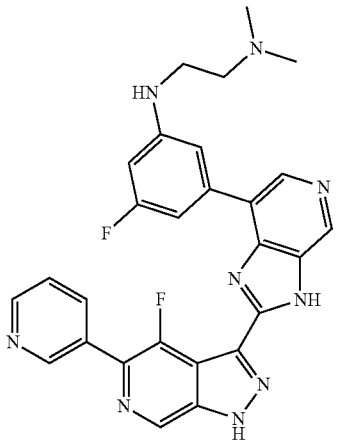
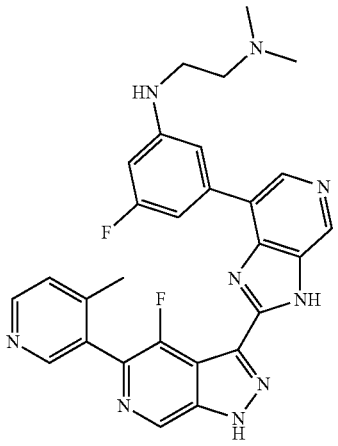
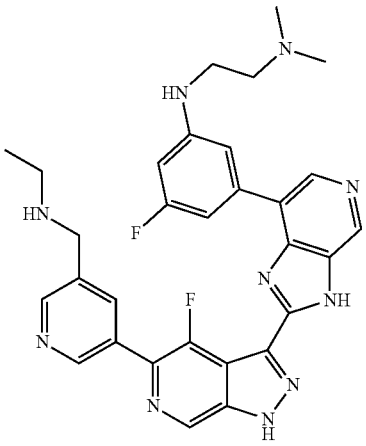
862	
863	
864	

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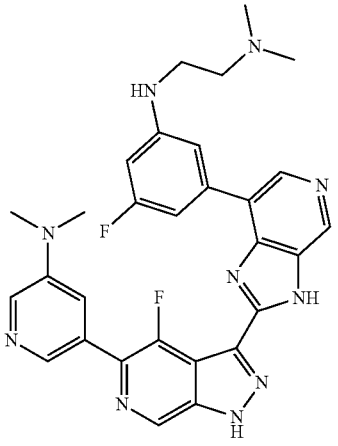
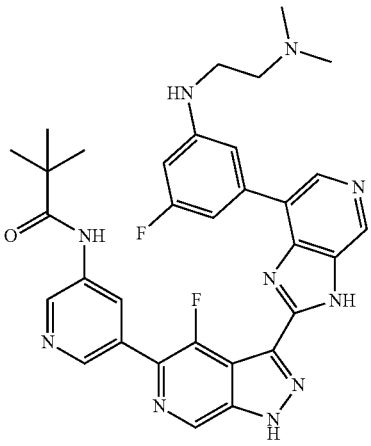
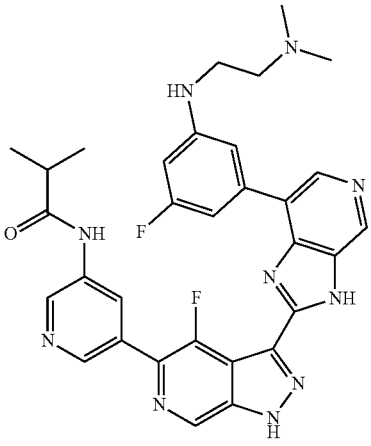
865	
866	
867	

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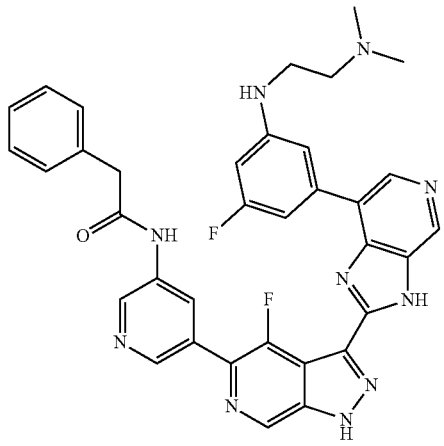
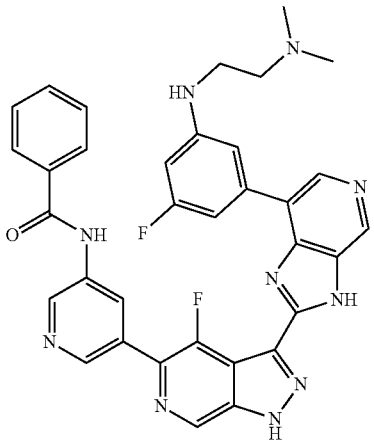
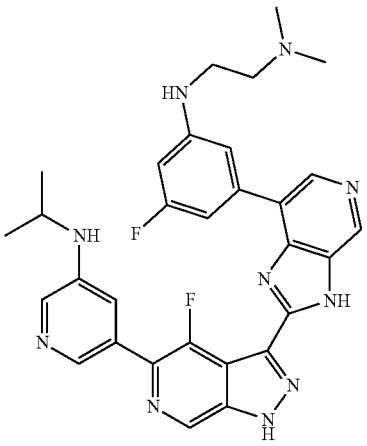
868	
869	
870	

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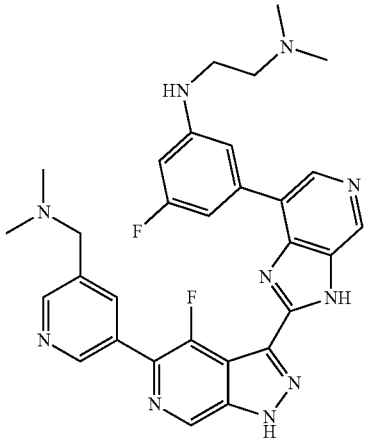
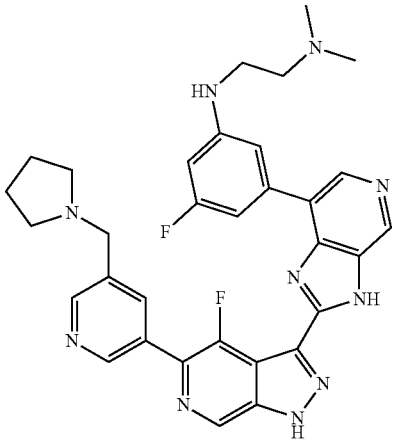
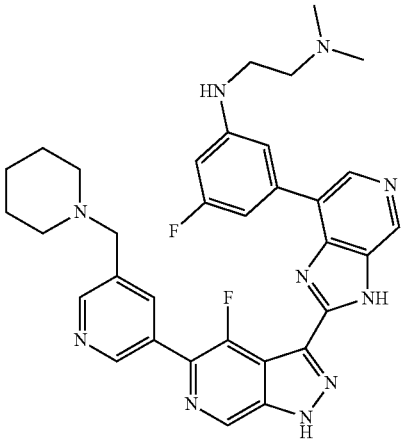
871	
872	
873	

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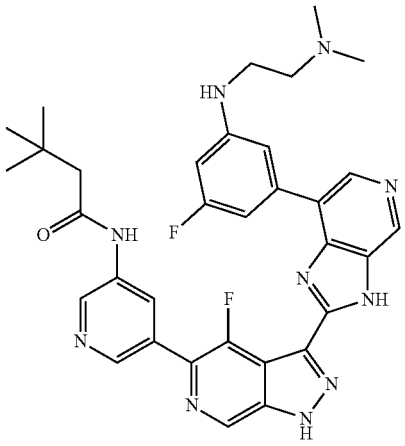
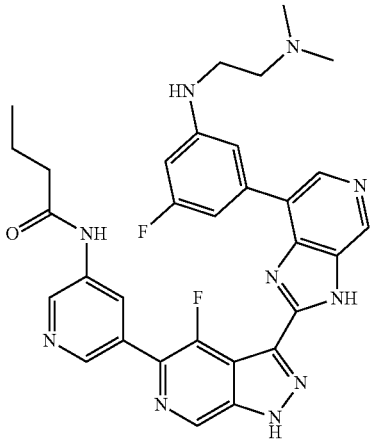
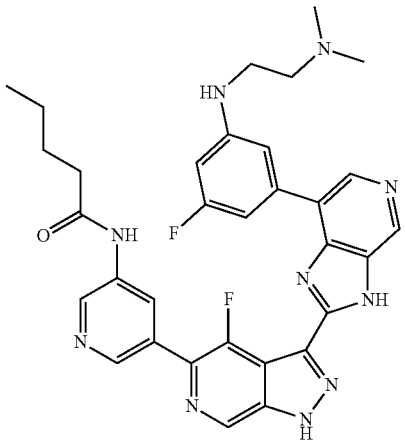
874	
875	
876	

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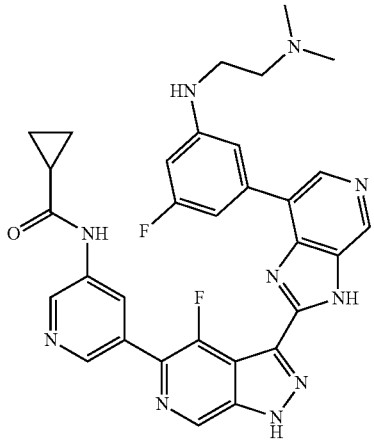
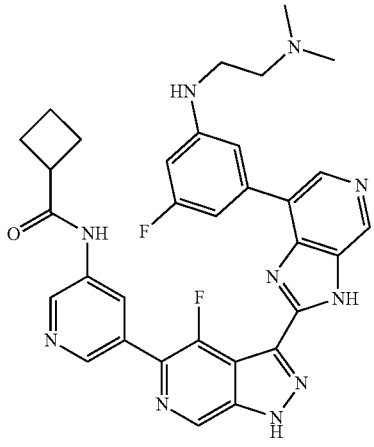
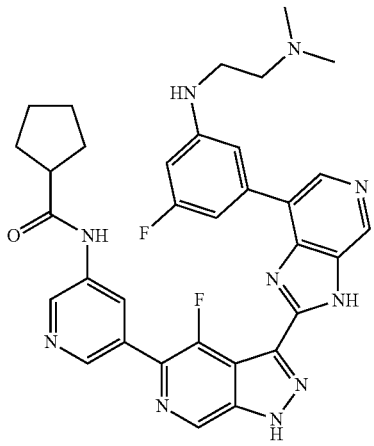
877	
878	
879	

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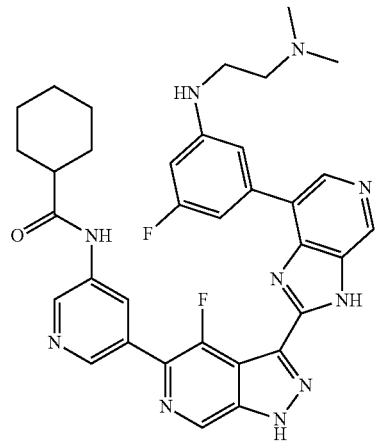
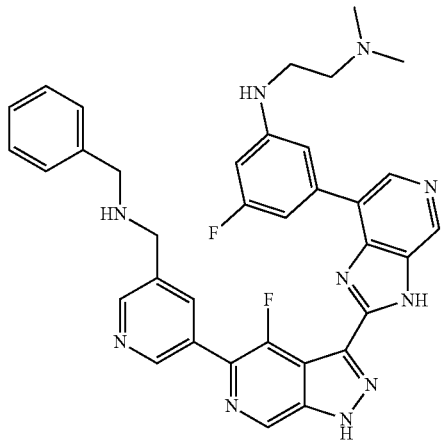
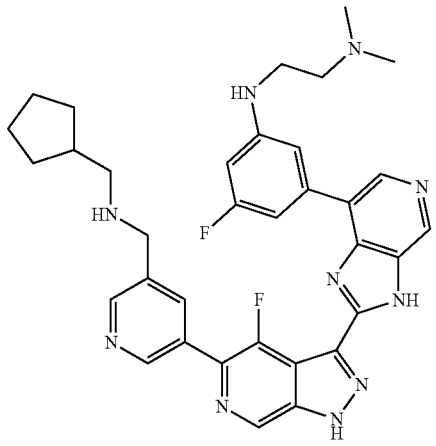
880	
881	
882	

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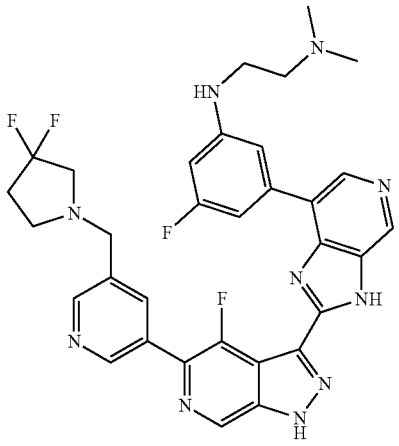
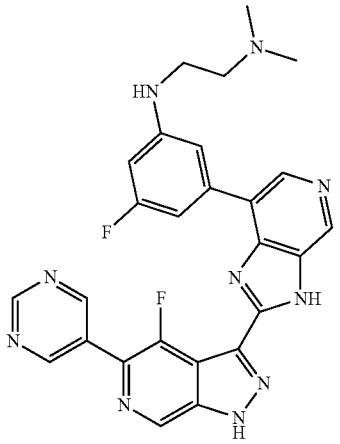
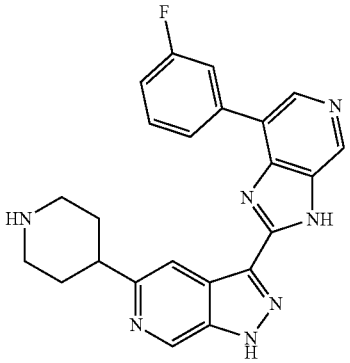
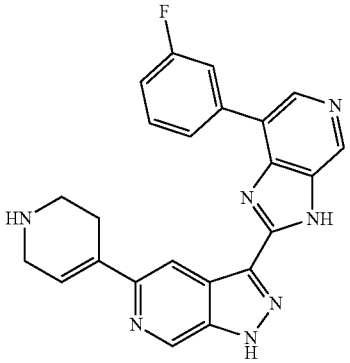
883	
884	
885	
886	

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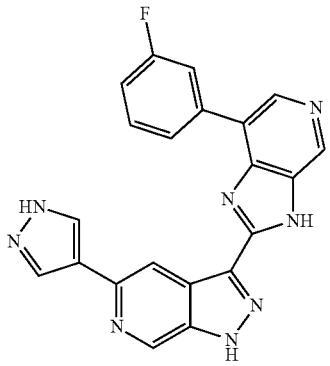
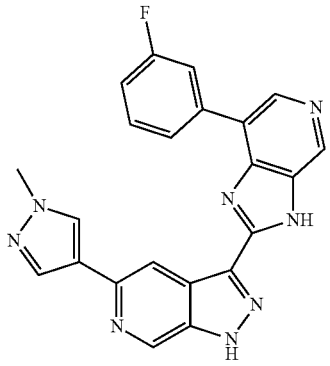
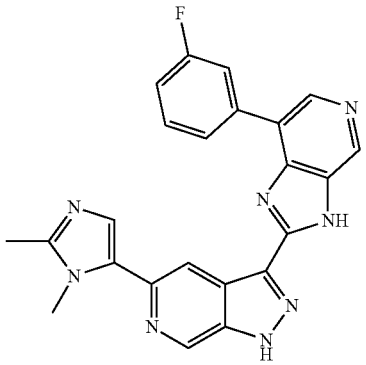
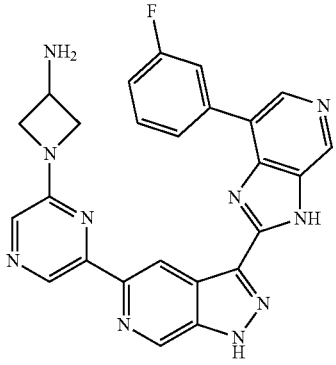
887	
888	
889	
890	

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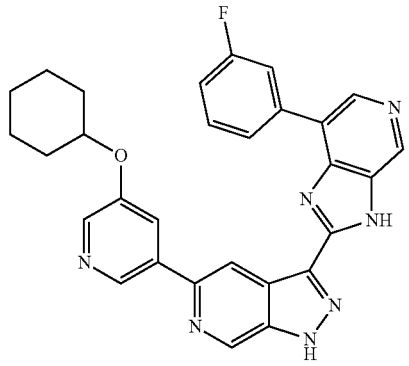
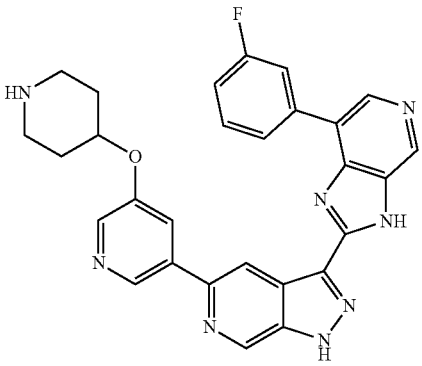
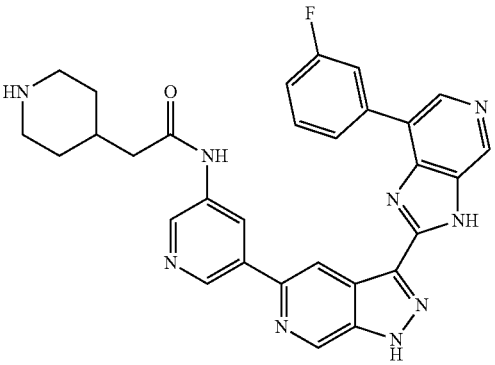
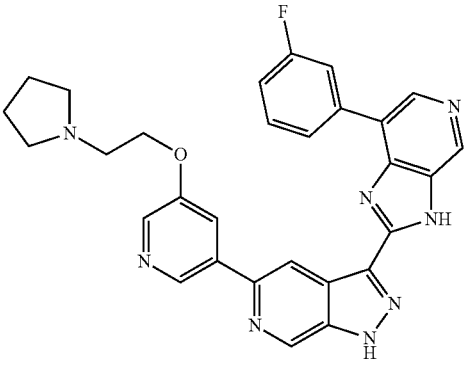
891	
892	
893	
894	

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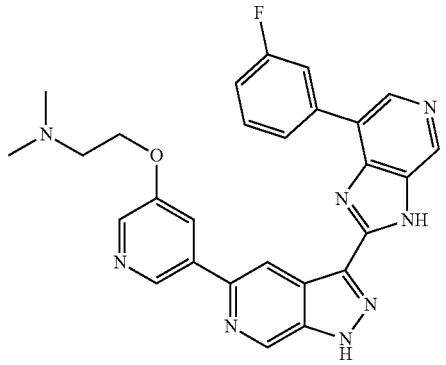
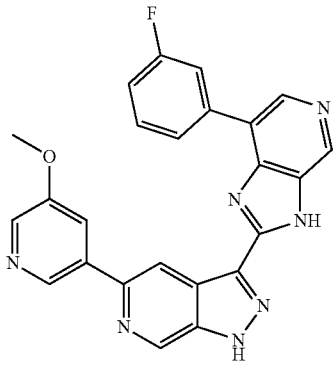
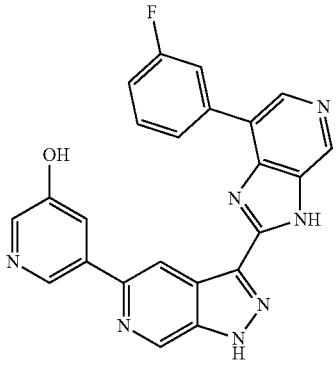
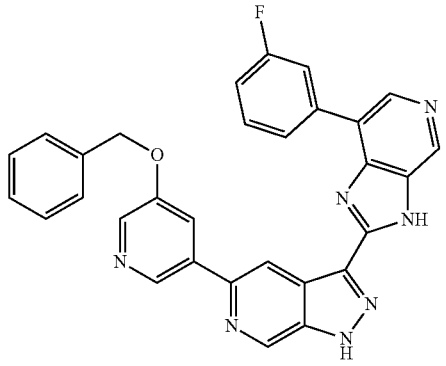
895	
896	
897	
898	

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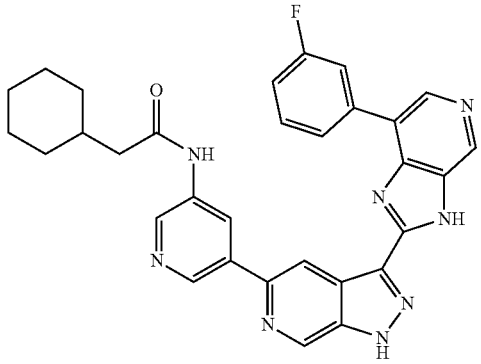
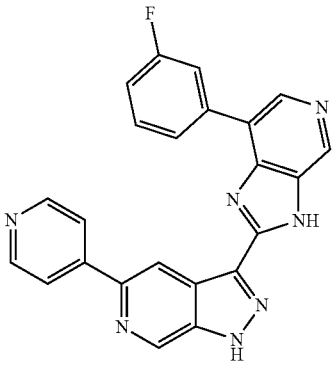
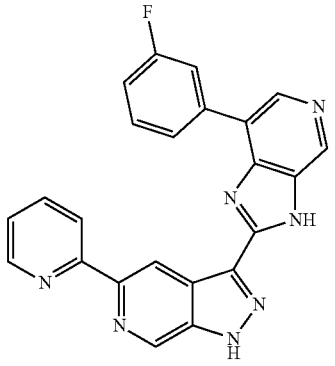
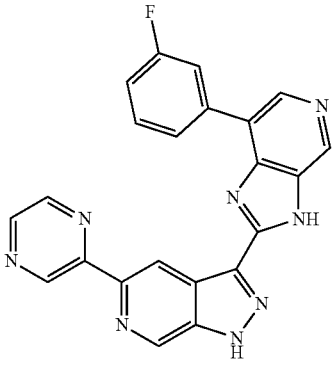
899	
900	
901	
902	

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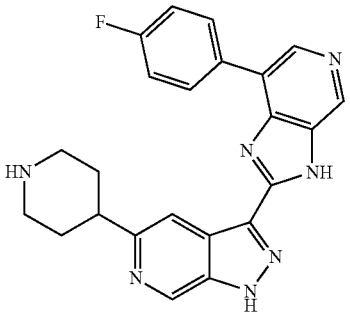
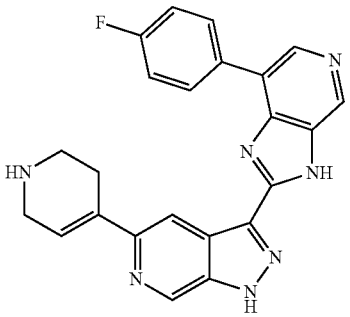
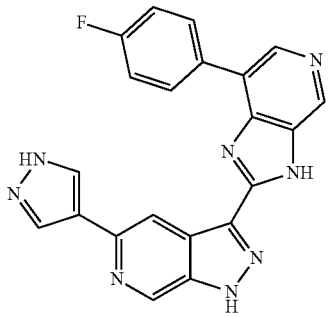
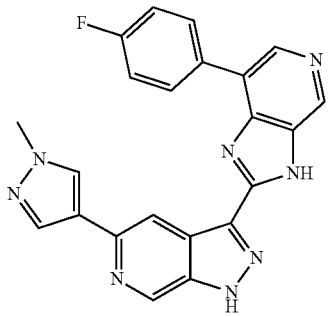
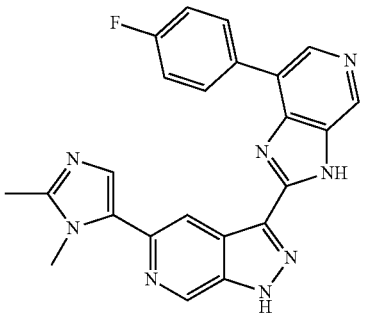
903	
904	
905	
906	
907	

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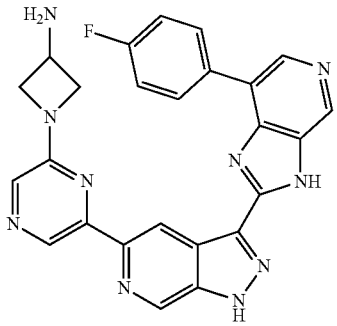
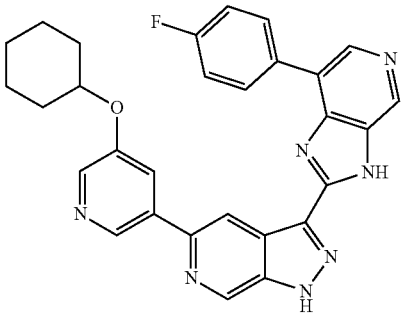
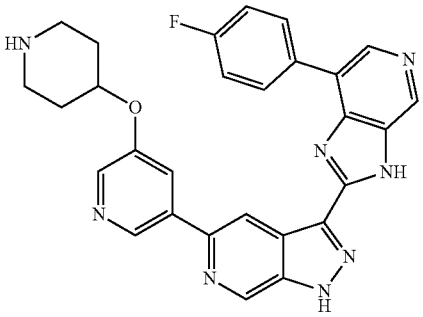
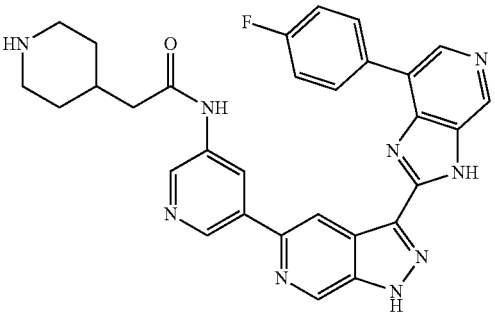
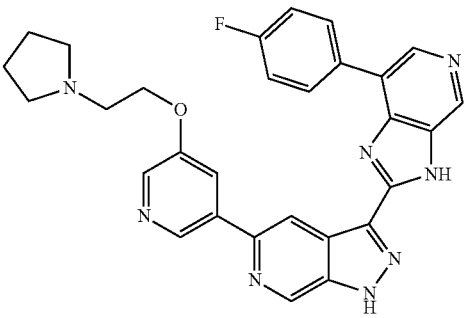
908	
909	
910	
911	
912	

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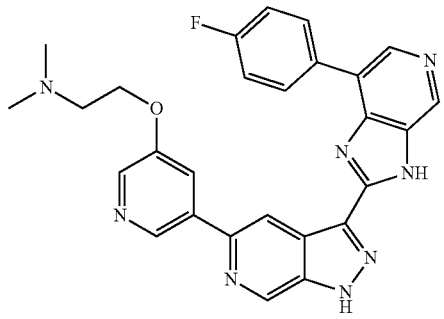
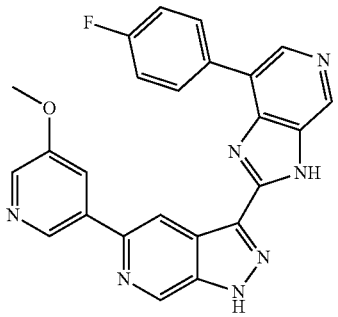
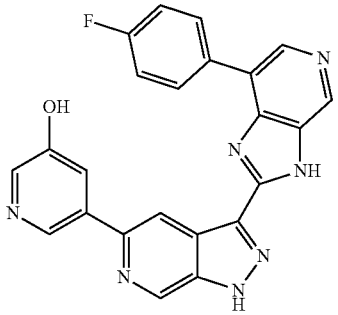
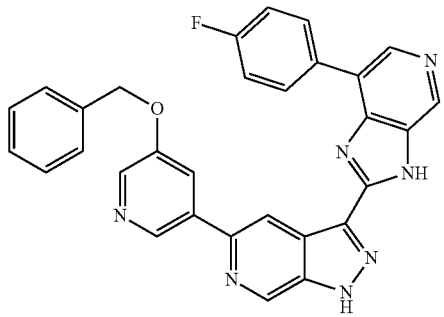
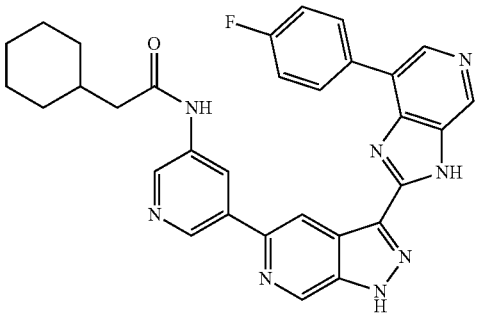
913	
914	
915	
916	
917	

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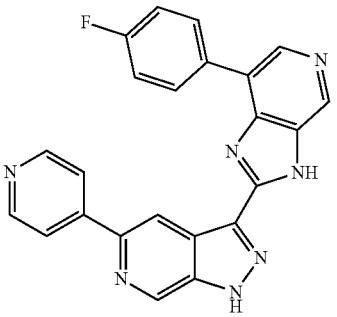
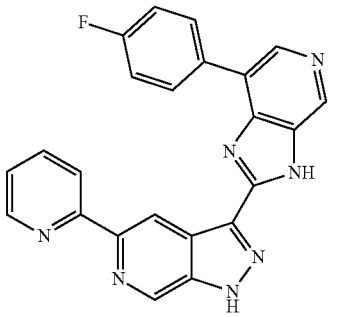
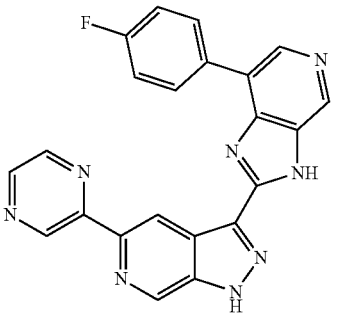
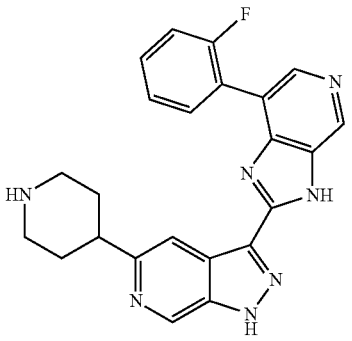
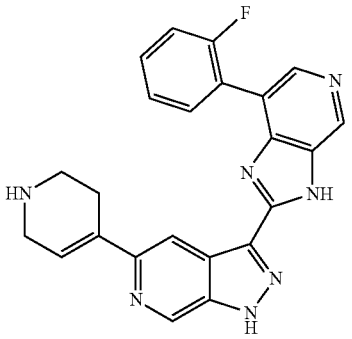
918	
919	
920	
921	
922	

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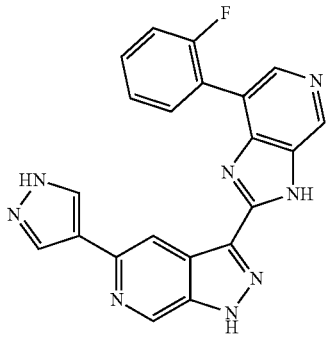
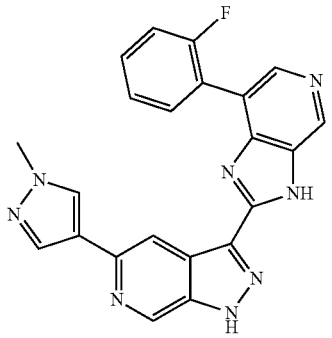
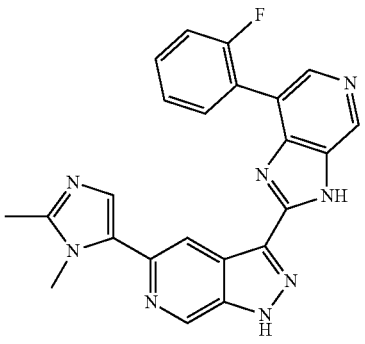
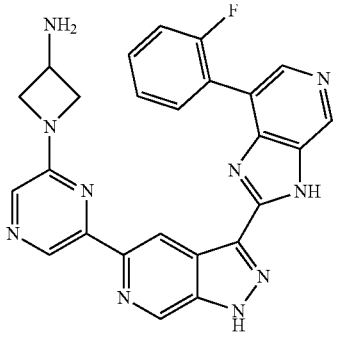
923	
924	
925	
926	

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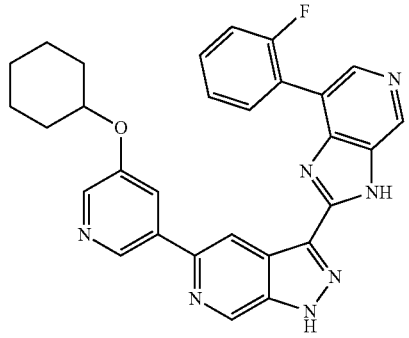
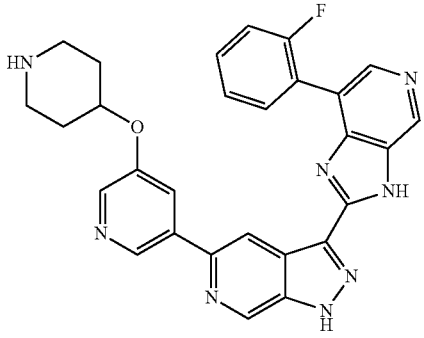
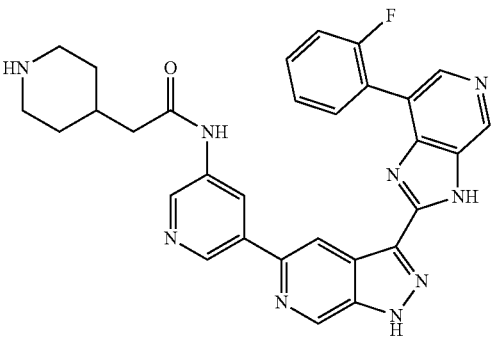
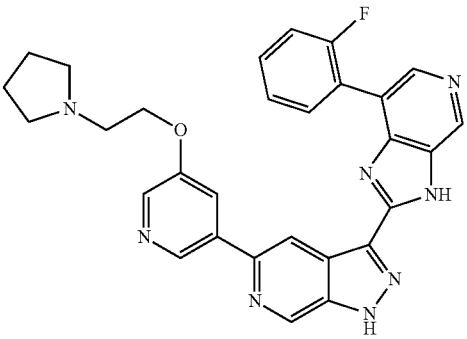
927	
928	
929	
930	

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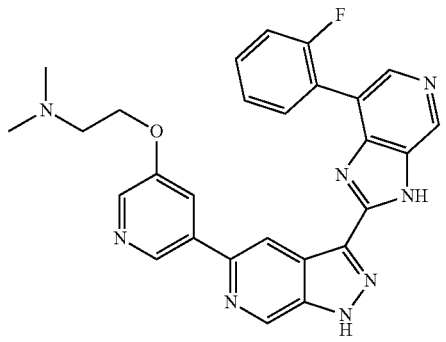
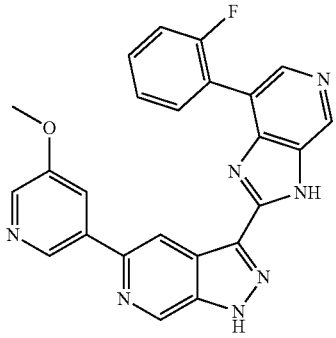
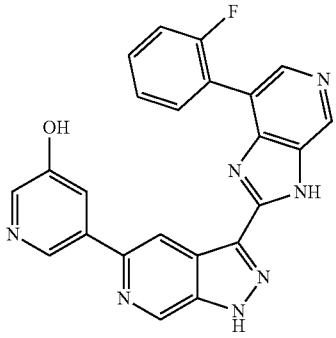
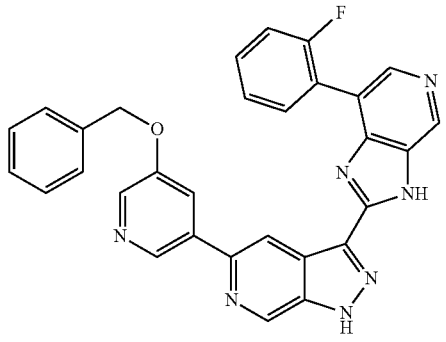
931	
932	
933	
934	

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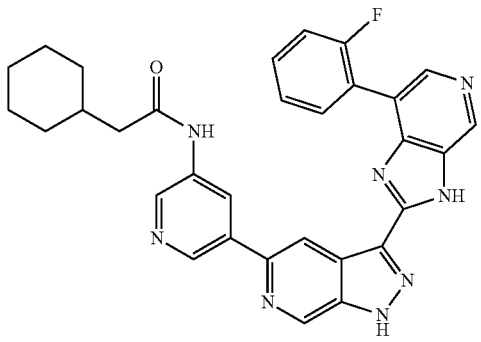
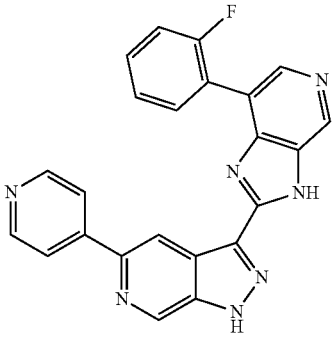
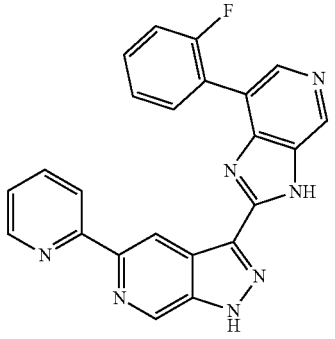
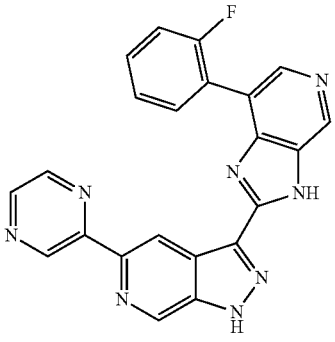
935	
936	
937	
938	

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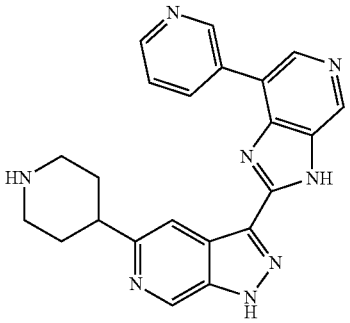
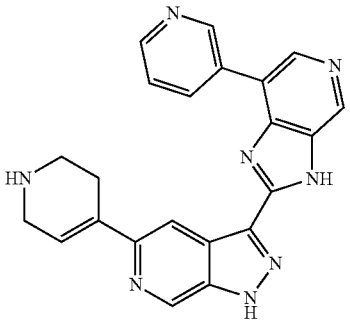
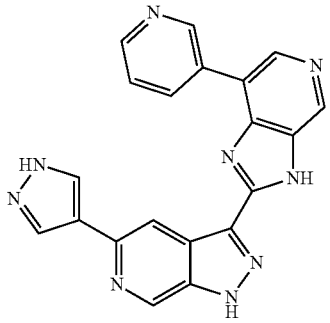
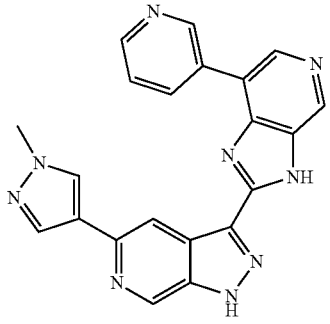
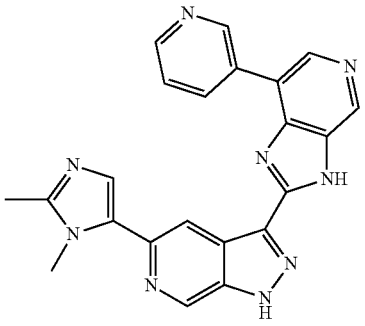
939	
940	
941	
942	
943	

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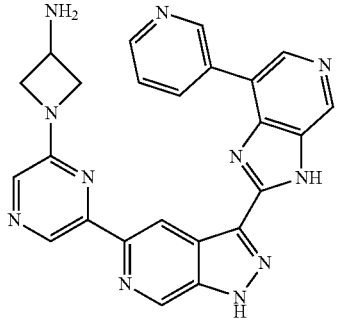
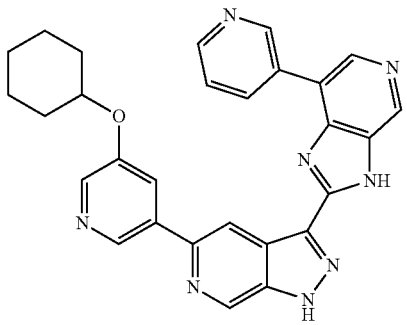
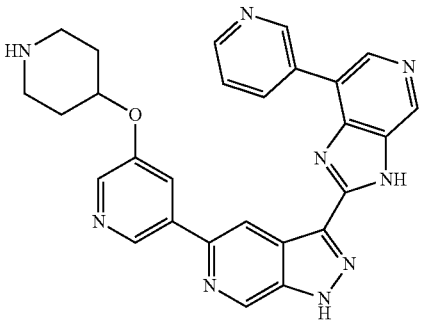
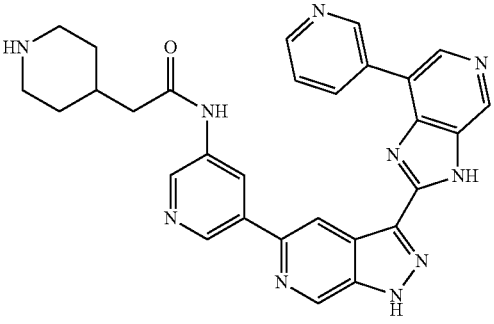
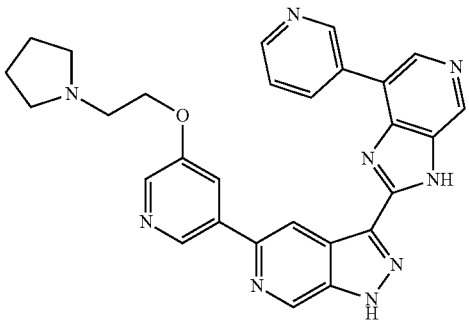
944	
945	
946	
947	
948	

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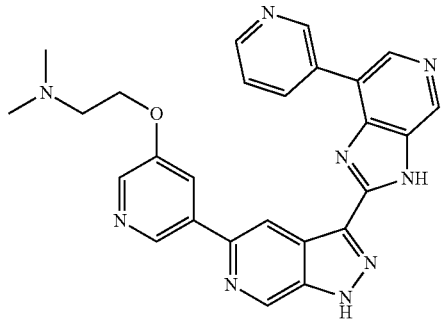
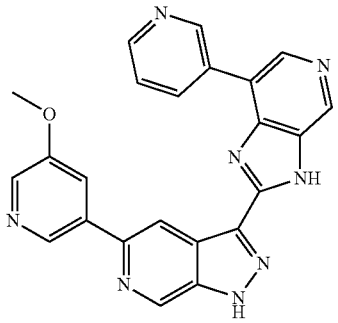
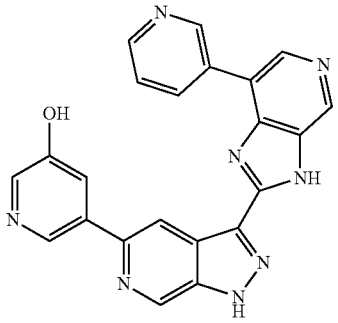
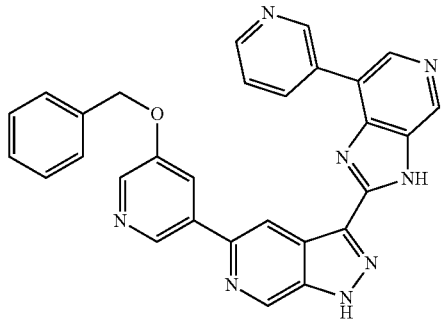
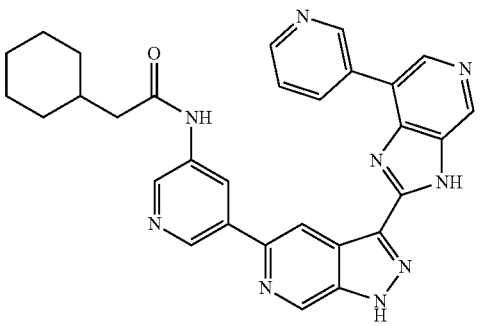
949	
950	
951	
952	
953	

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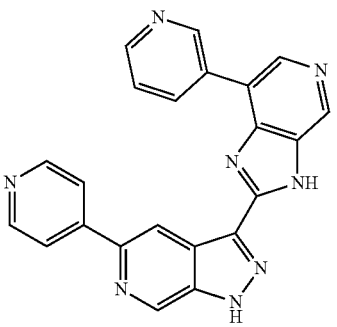
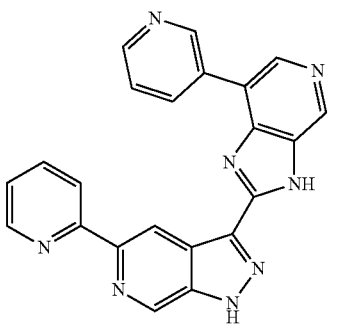
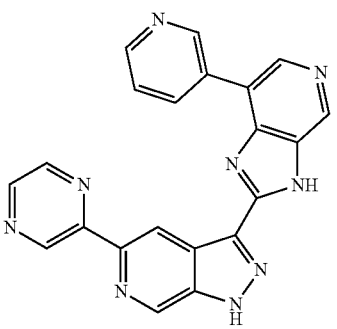
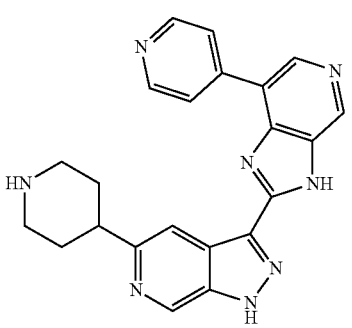
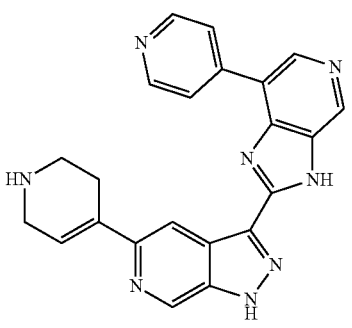
954	
955	
956	
957	
958	

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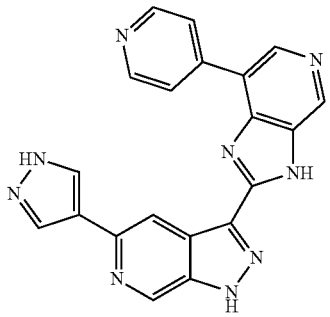
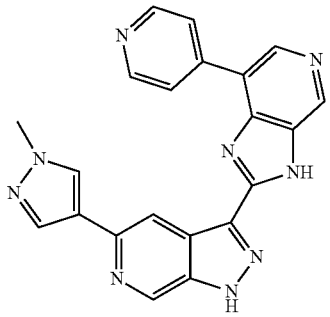
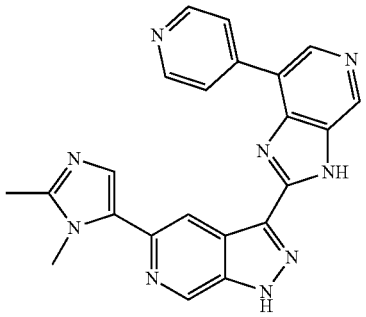
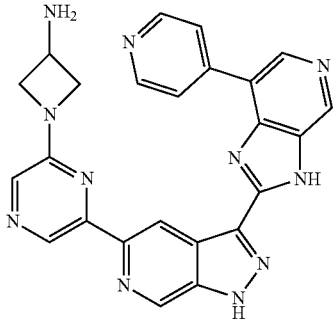
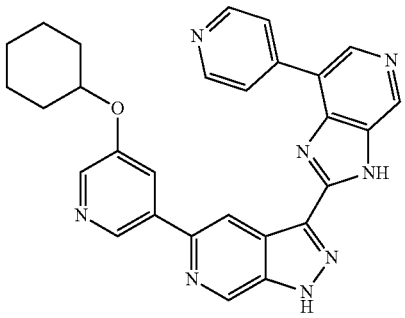
959	
960	
961	
962	
963	

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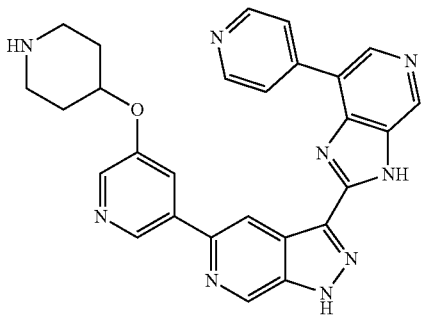
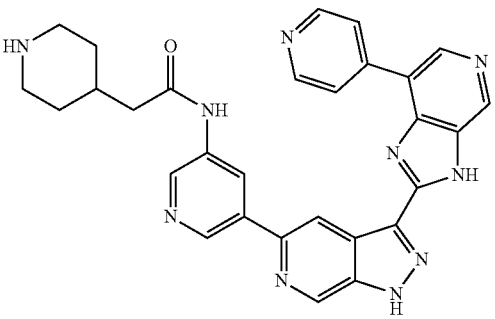
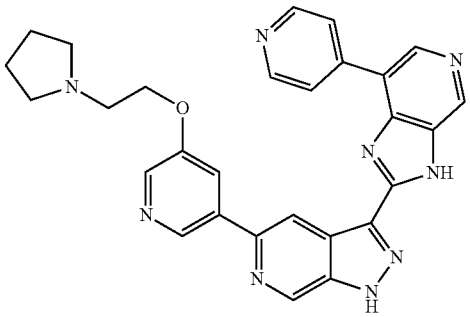
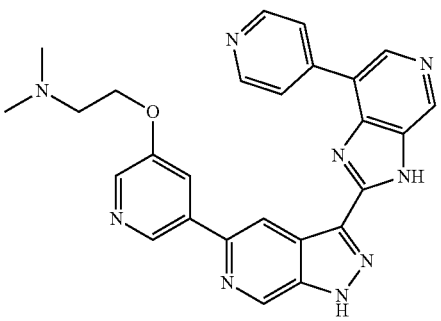
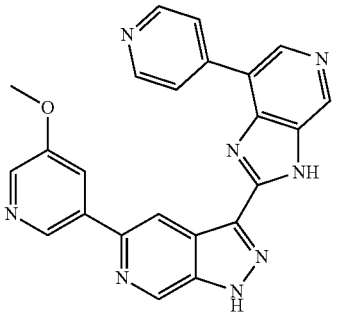
964	
965	
966	
967	
968	

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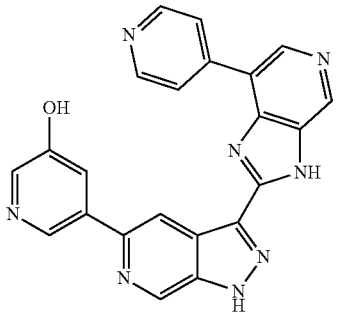
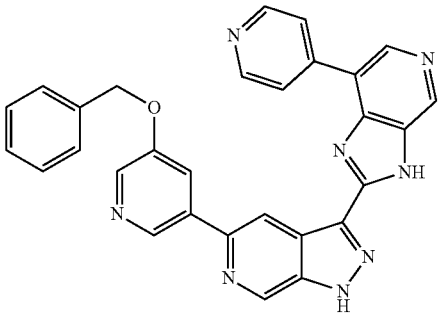
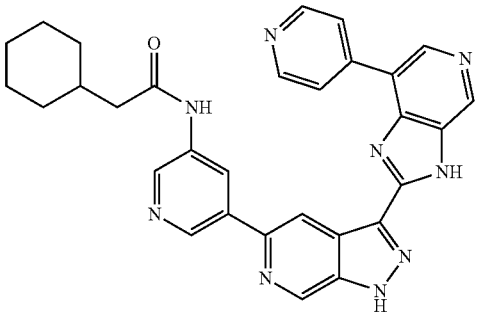
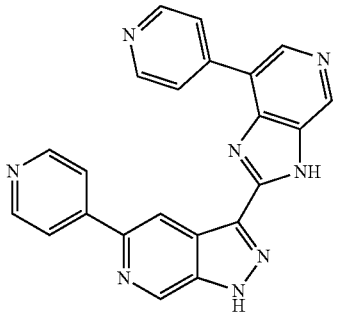
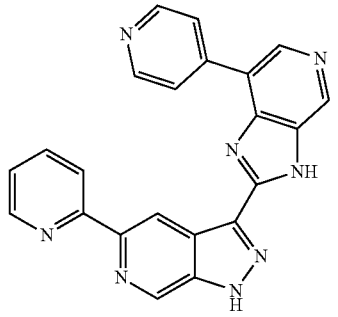
969	
970	
971	
972	
973	

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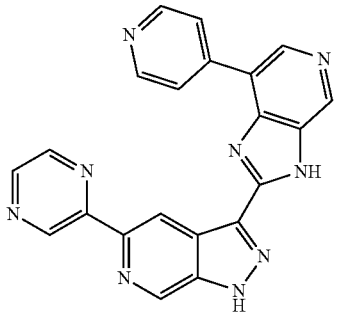
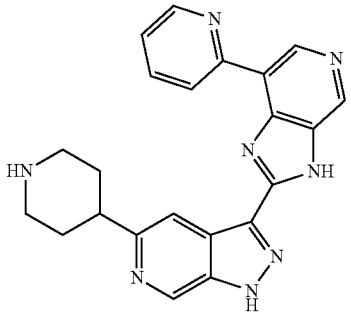
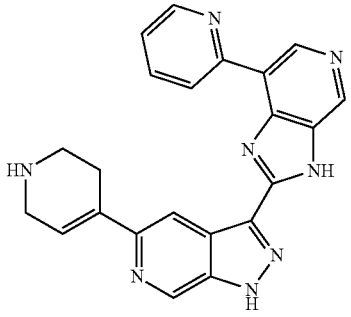
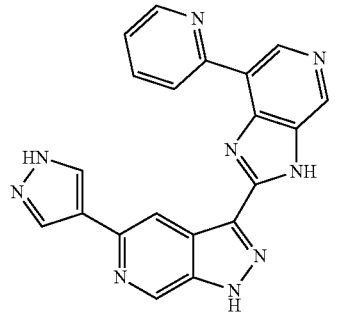
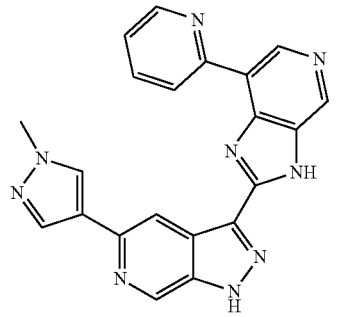
974	
975	
976	
977	
978	

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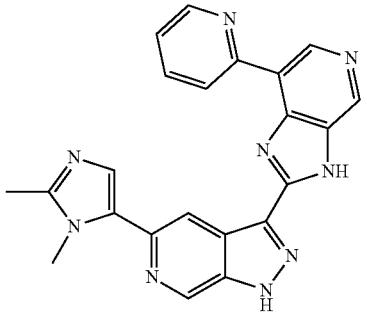
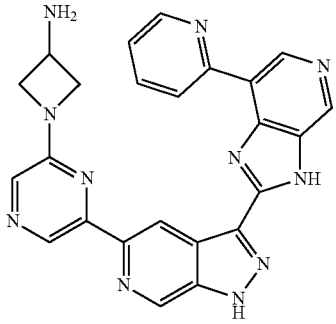
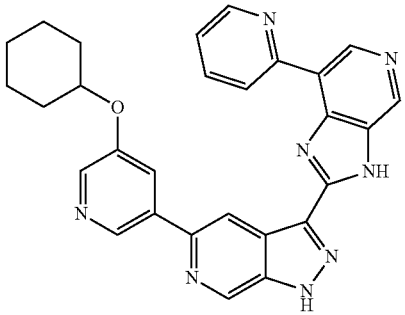
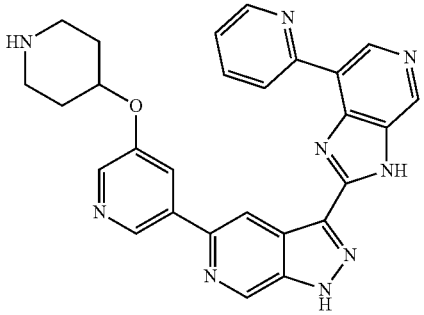
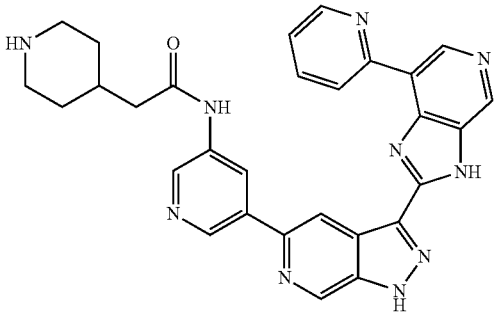
979	
980	
981	
982	
983	

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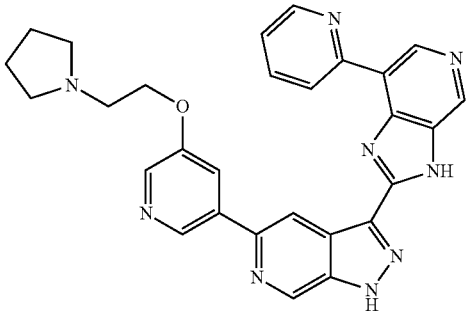
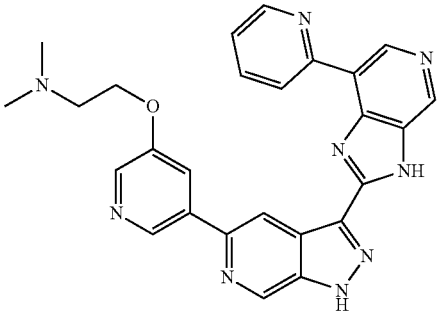
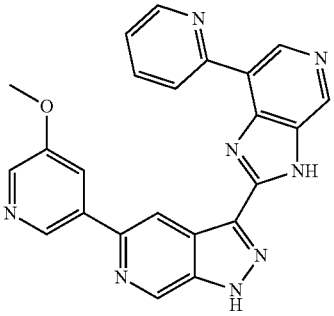
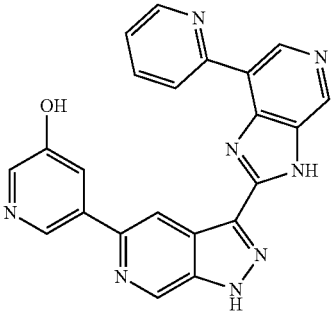
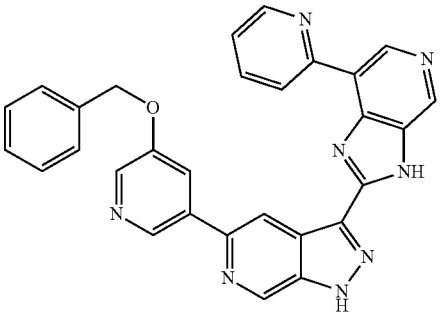
984	
985	
986	
987	
988	

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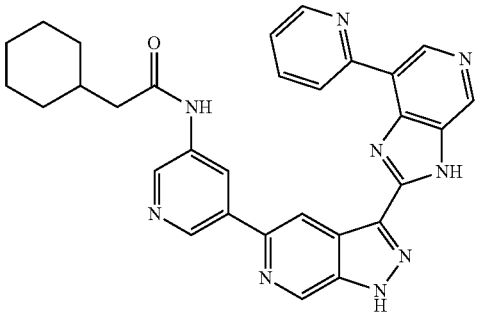
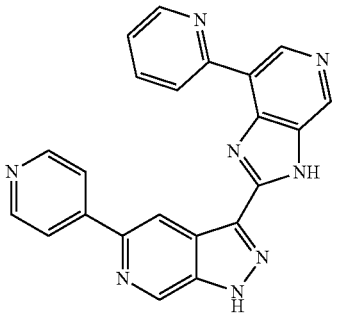
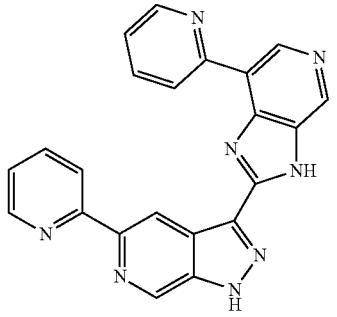
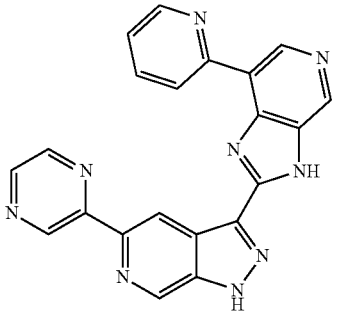
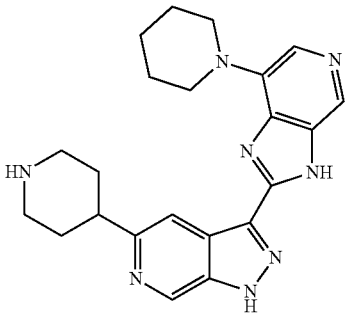
989	
990	
991	
992	
993	

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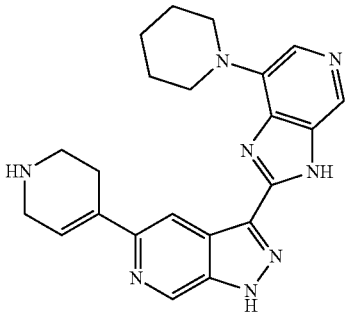
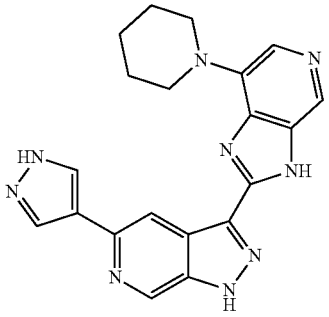
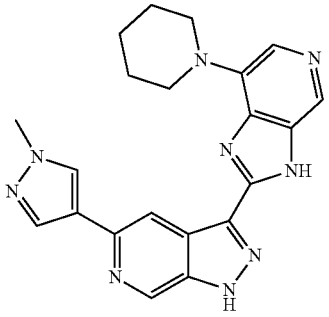
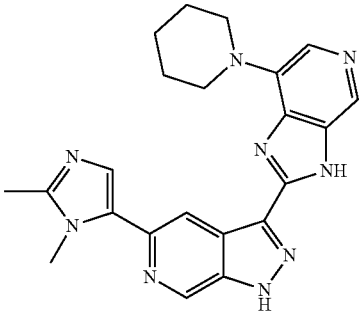
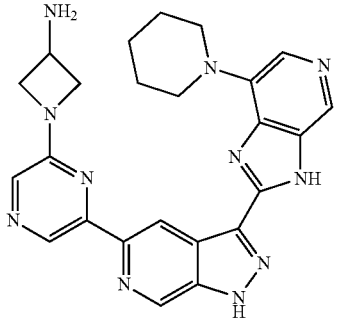
994	
995	
996	
997	
998	

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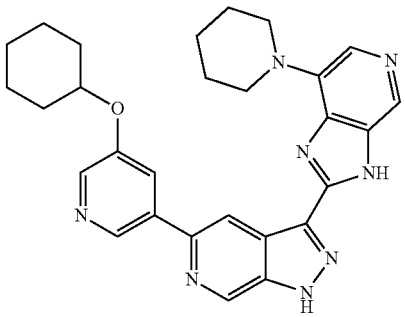
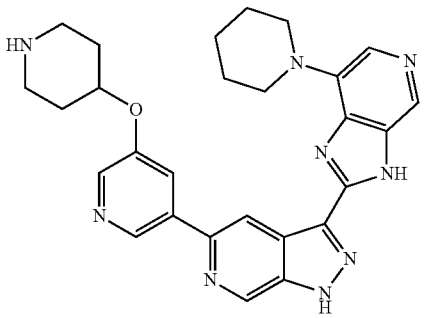
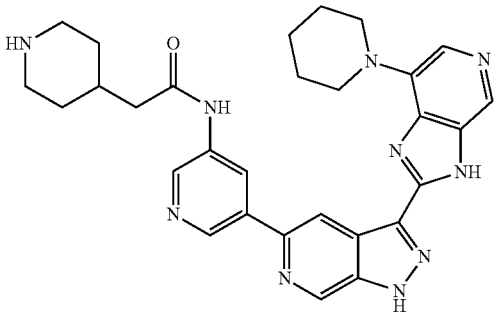
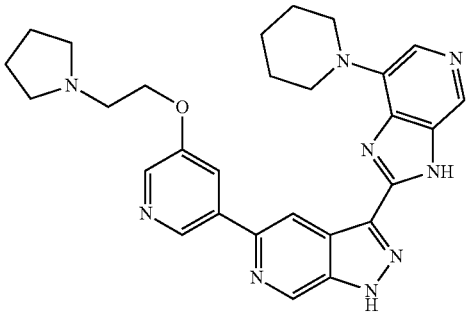
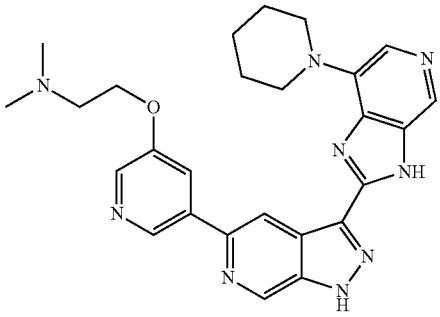
999	
1000	
1001	
1002	
1003	

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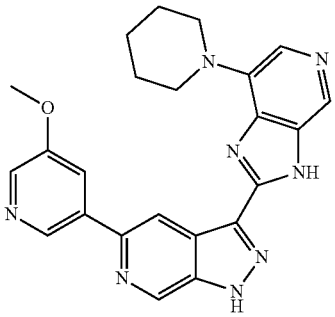
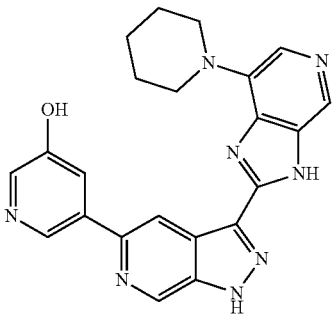
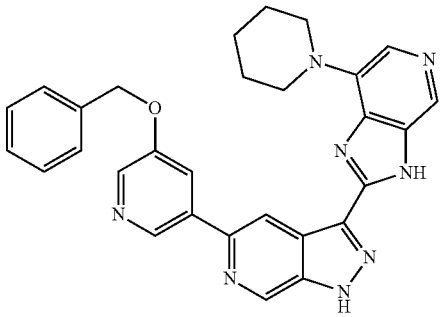
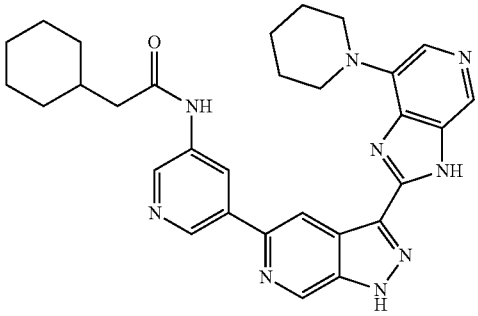
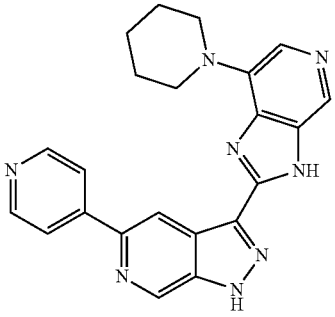
1004	
1005	
1006	
1007	
1008	

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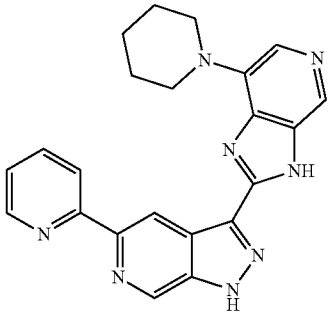
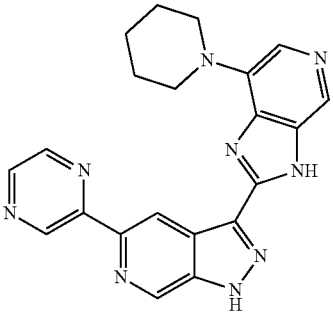
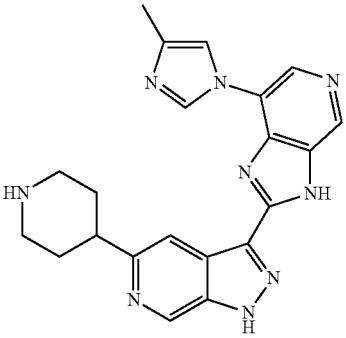
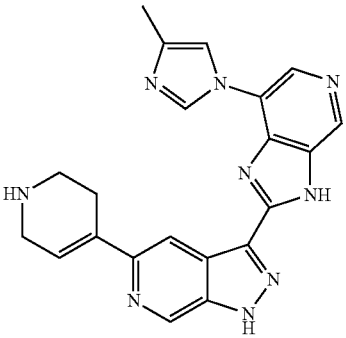
1009	
1010	
1011	
1012	

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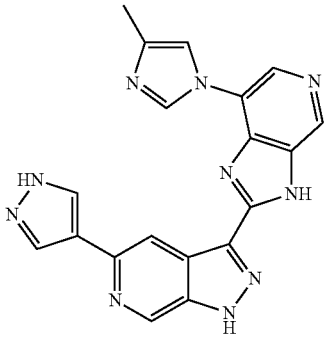
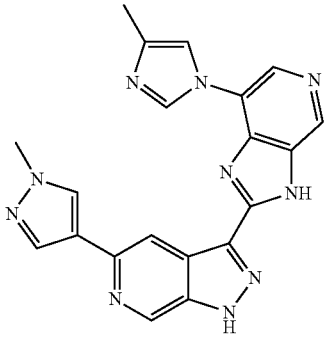
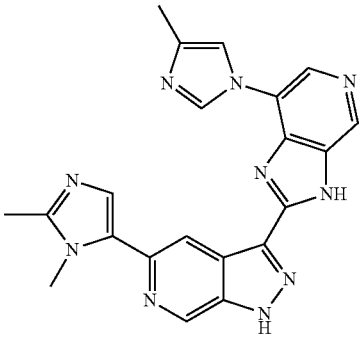
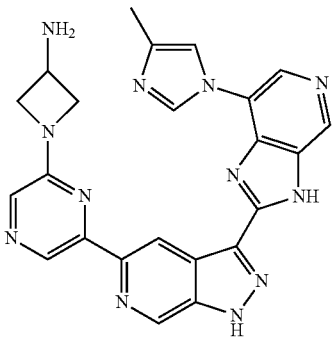
1013	
1014	
1015	
1016	

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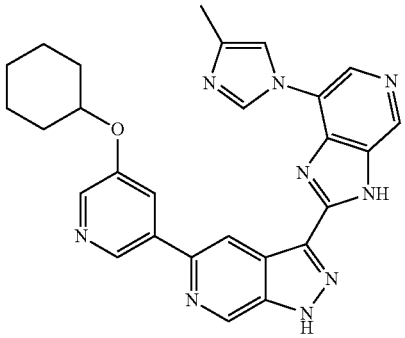
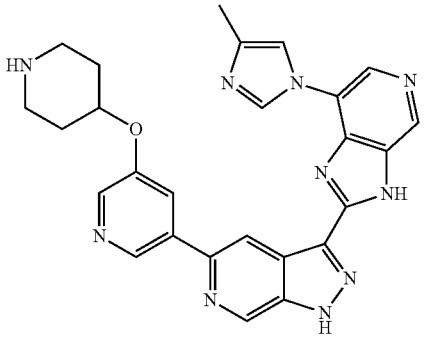
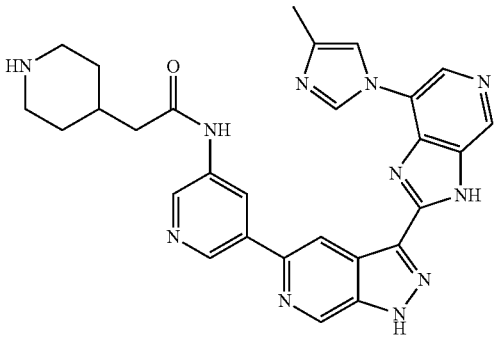
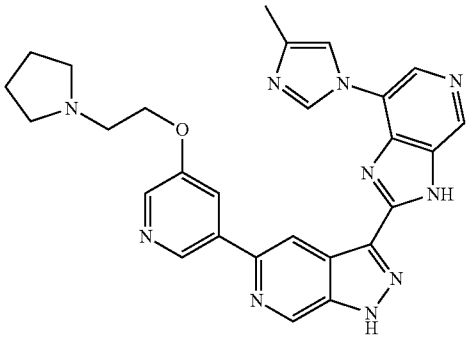
1017	
1018	
1019	
1020	

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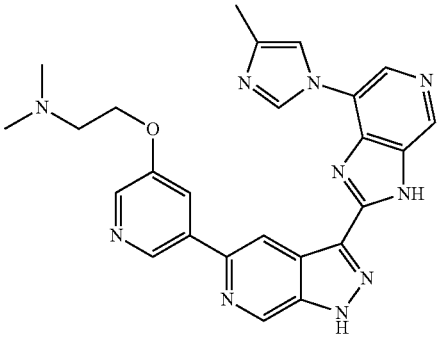
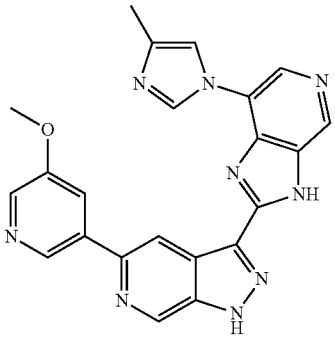
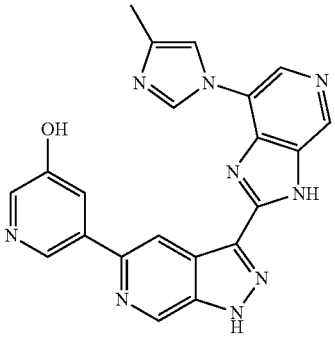
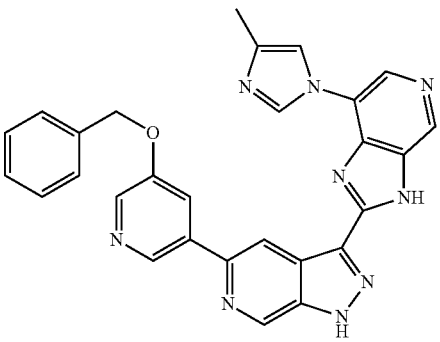
1021	
1022	
1023	
1024	

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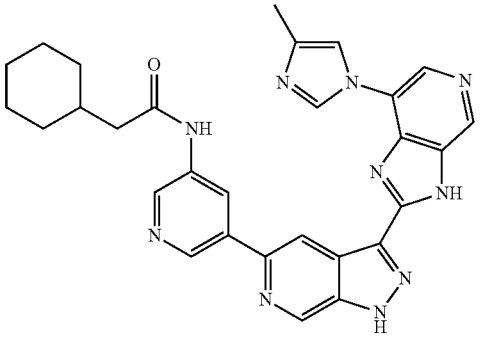
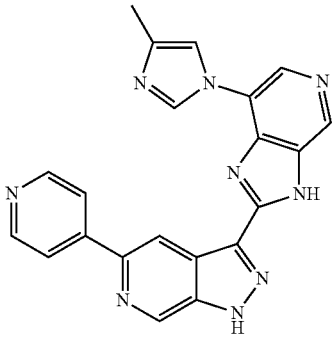
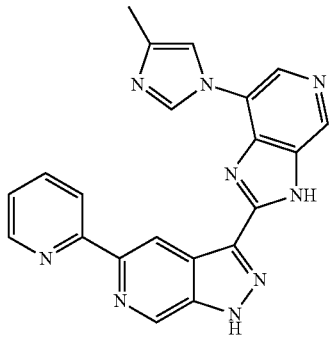
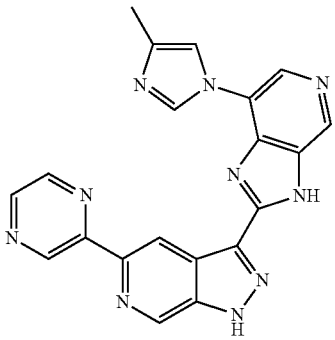
1025	
1026	
1027	
1028	

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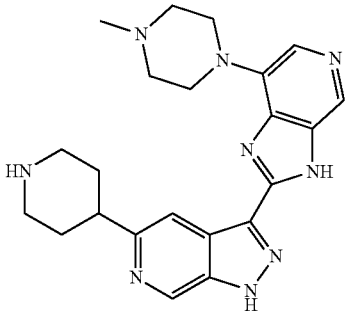
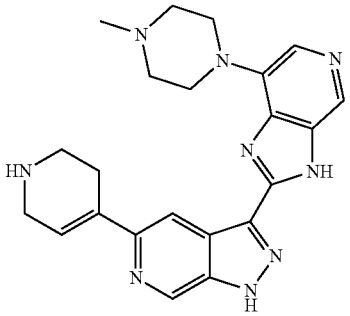
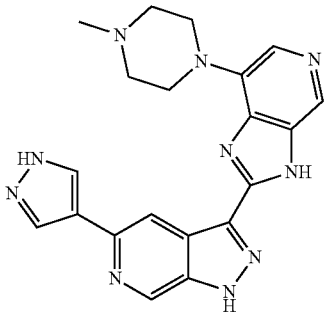
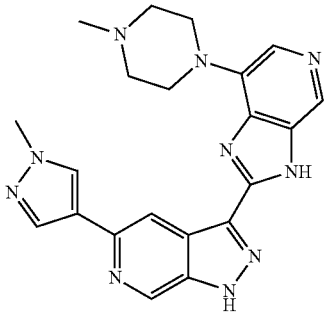
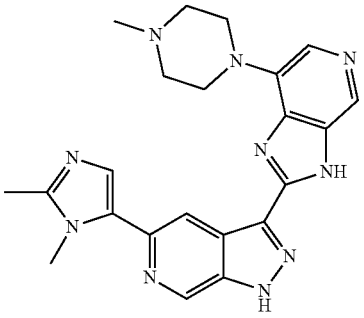
1029	
1030	
1031	
1032	
1033	

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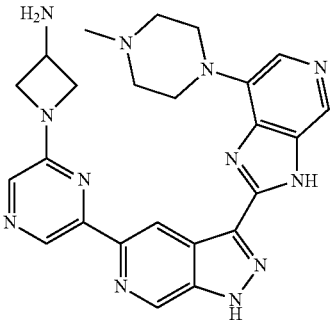
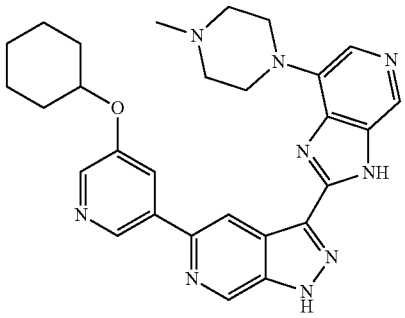
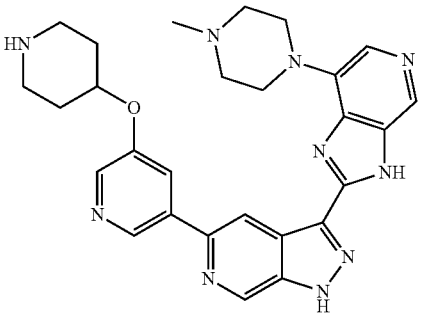
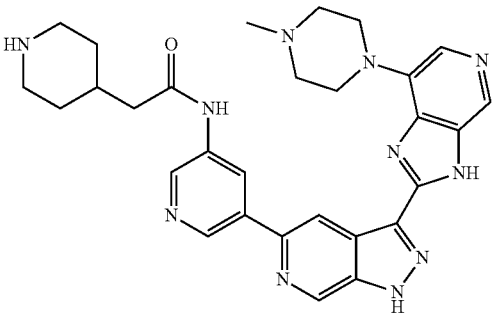
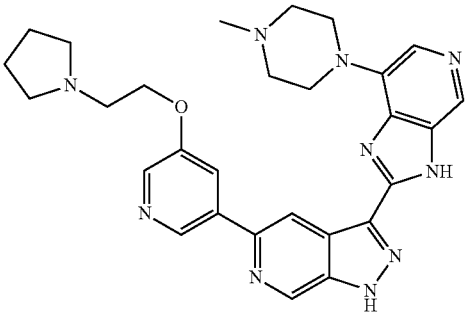
1034	
1035	
1036	
1037	
1038	

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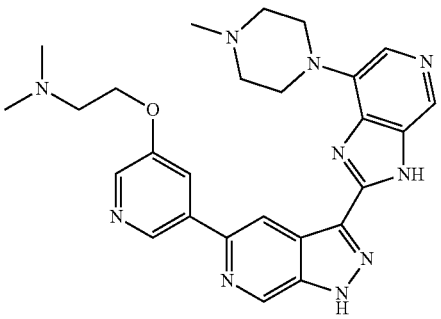
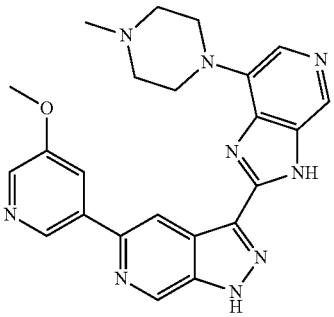
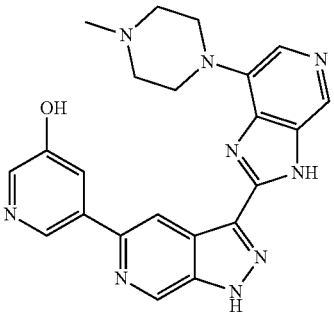
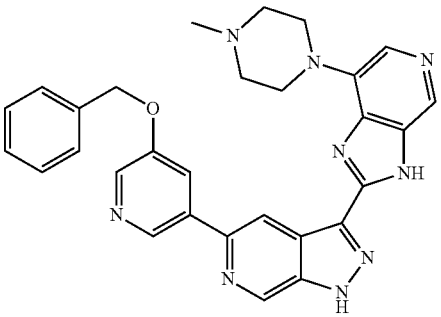
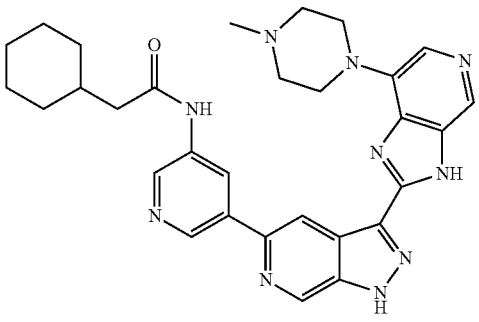
1039	
1040	
1041	
1042	
1043	

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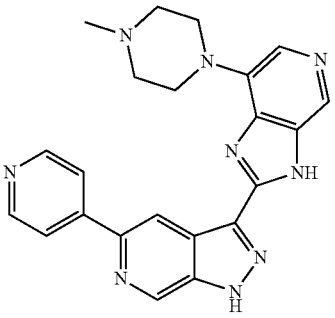
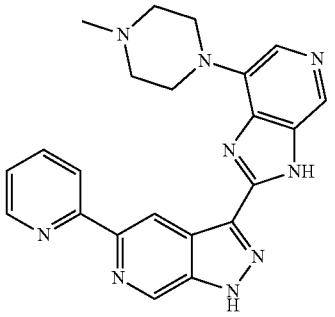
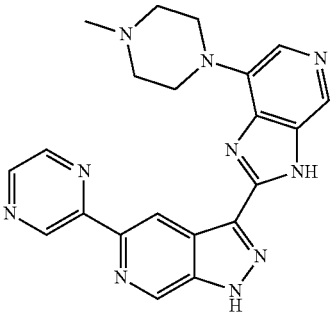
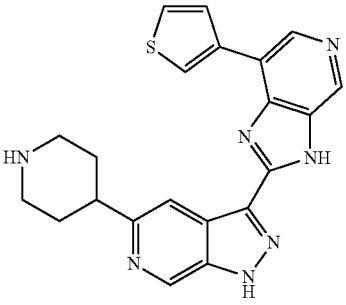
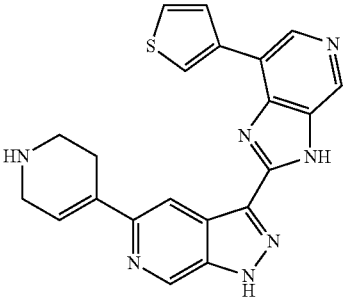
1044	
1045	
1046	
1047	
1048	

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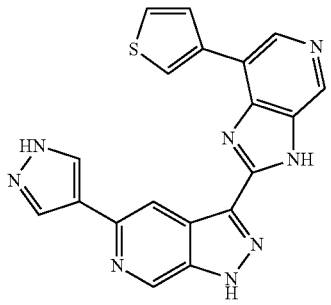
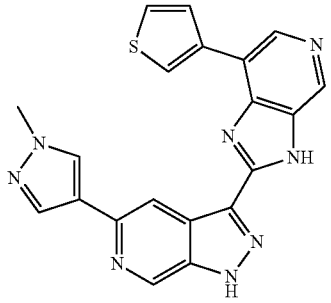
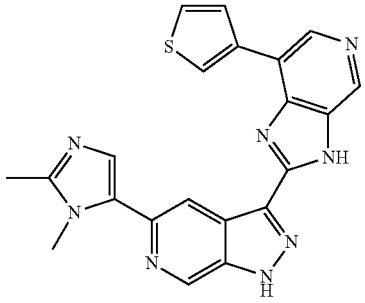
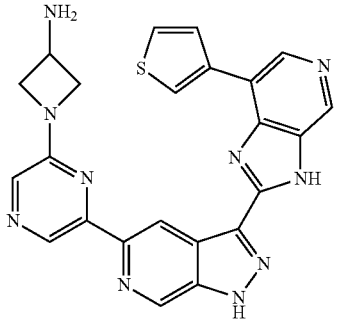
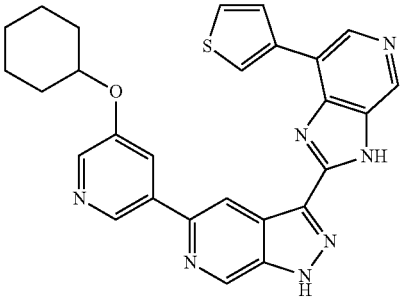
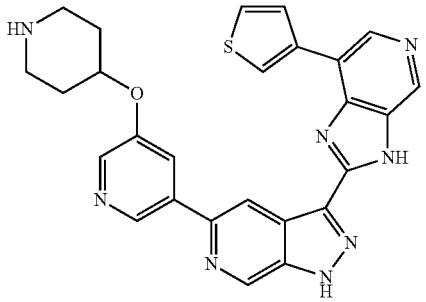
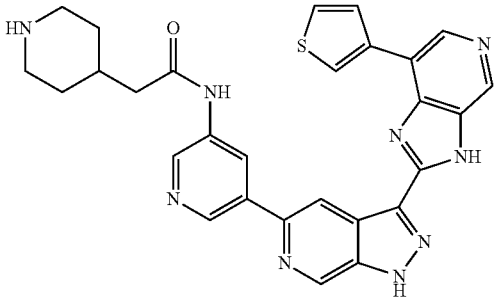
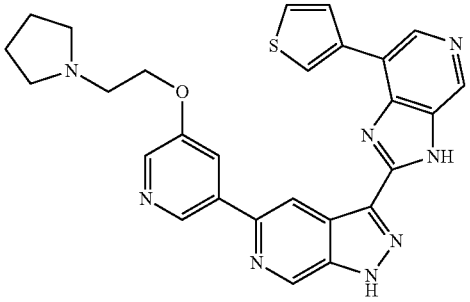
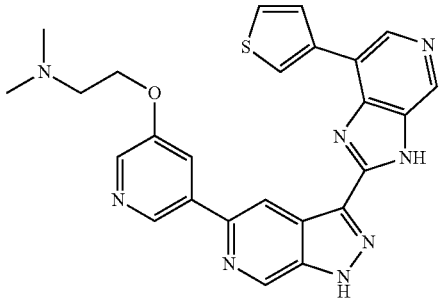
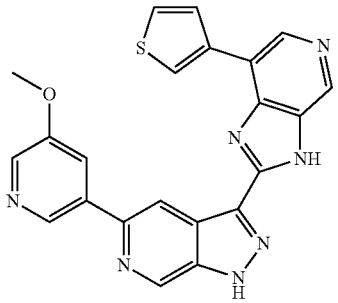
1049	
1050	
1051	
1052	
1053	

TABLE 1-continued

1054	
1055	
1056	
1057	
1058	

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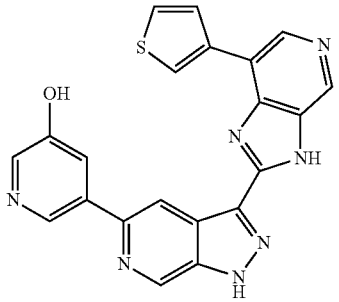
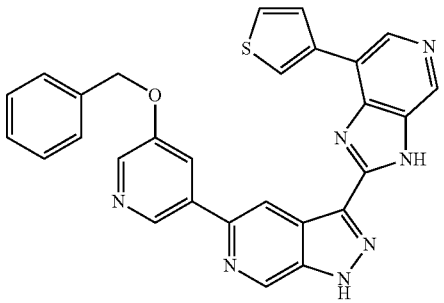
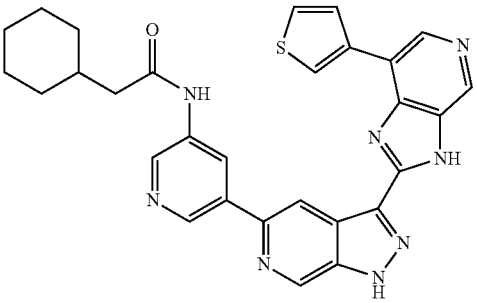
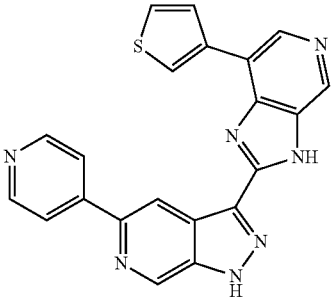
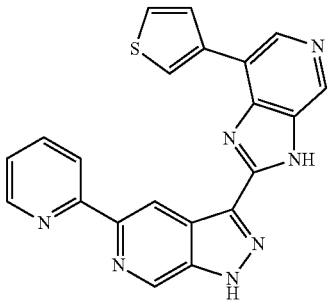
1059	
1060	
1061	
1062	
1063	

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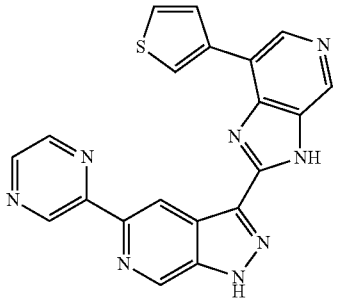
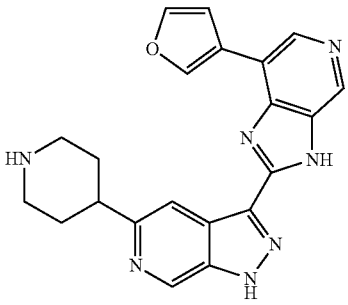
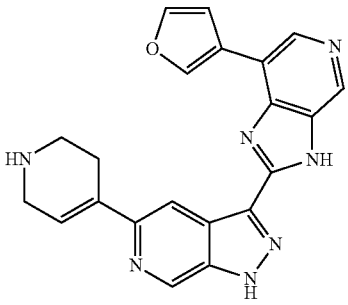
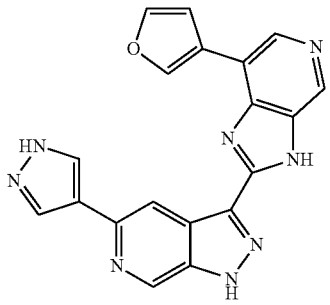
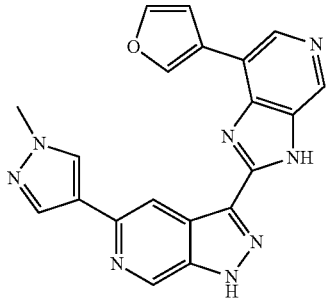
1064	
1065	
1066	
1067	
1068	

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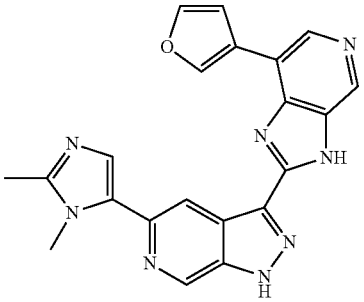
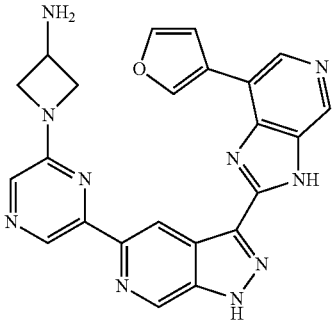
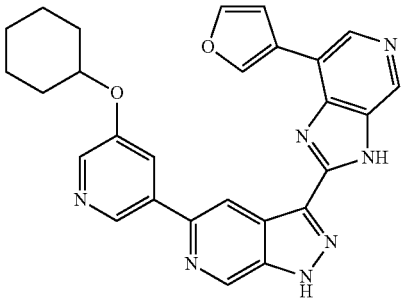
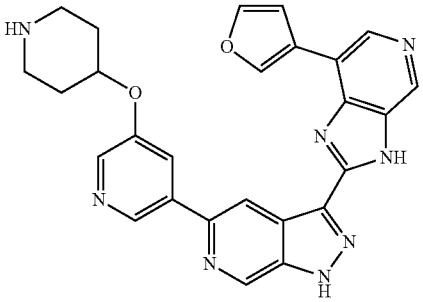
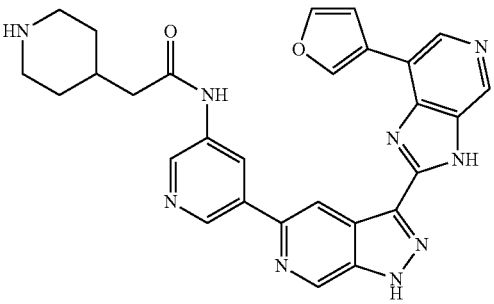
1069	
1070	
1071	
1072	
1073	

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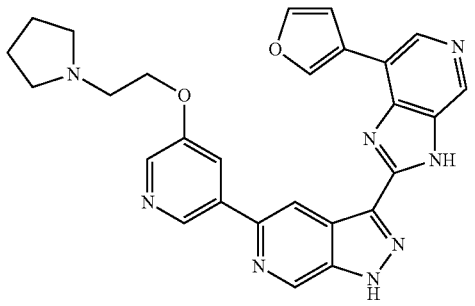
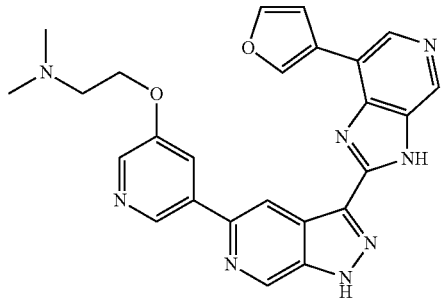
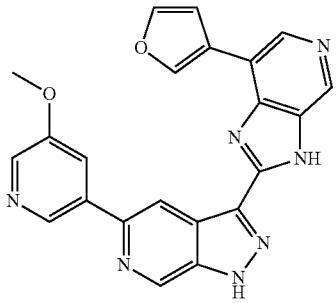
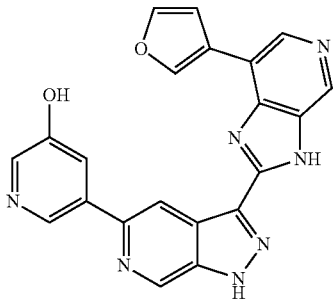
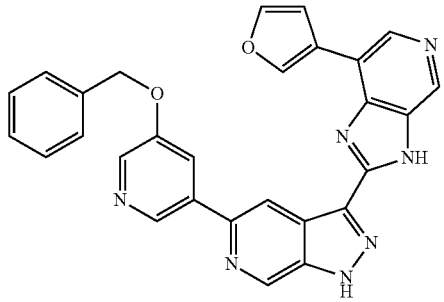
1074	
1075	
1076	
1077	
1078	

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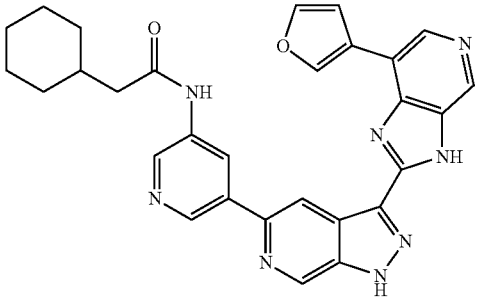
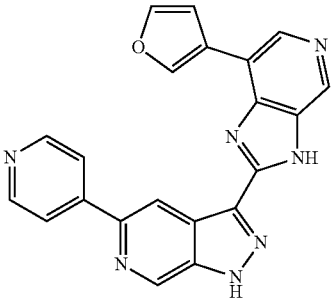
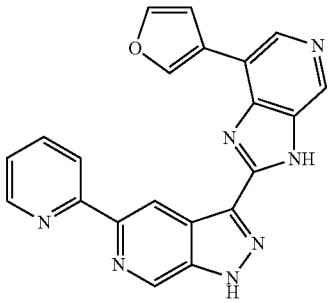
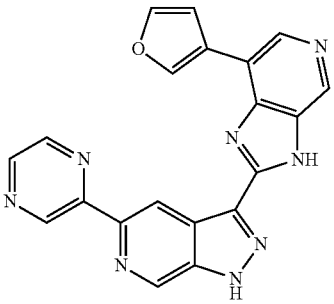
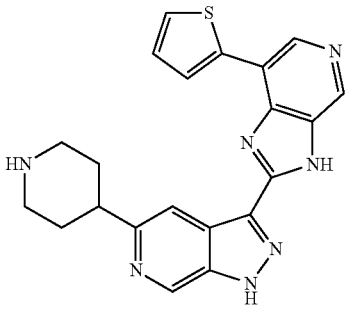
1079	
1080	
1081	
1082	
1083	

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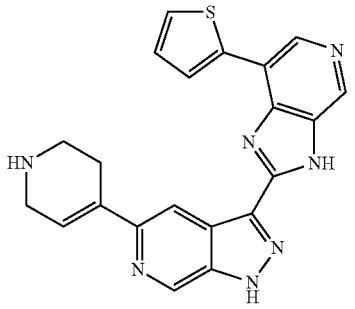
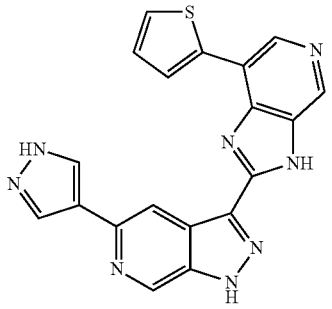
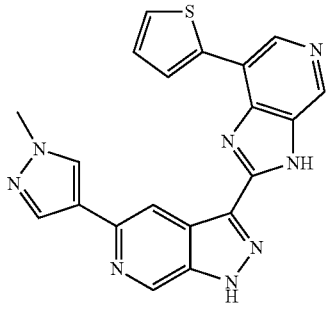
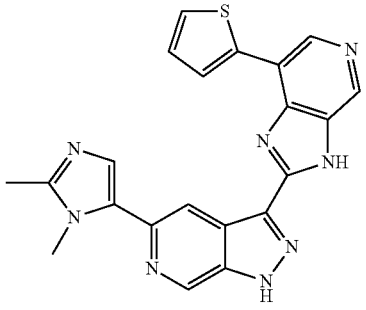
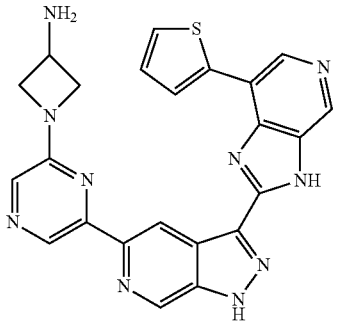
1084	
1085	
1086	
1087	
1088	

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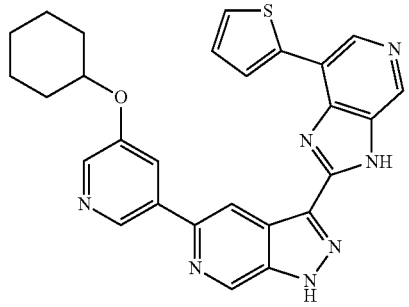
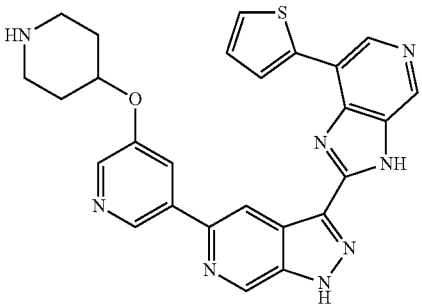
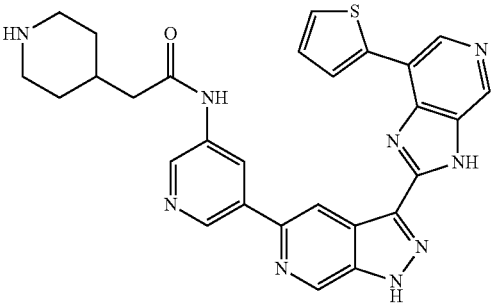
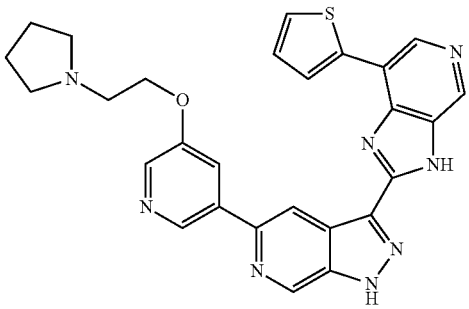
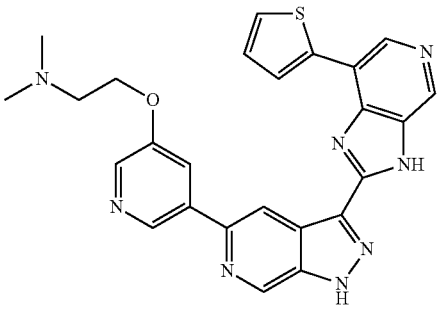
1089	
1090	
1091	
1092	
1093	

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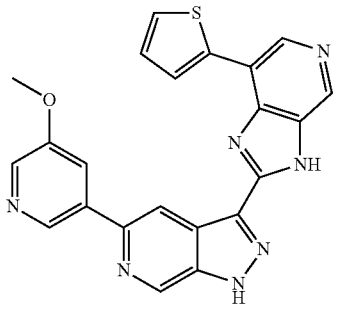
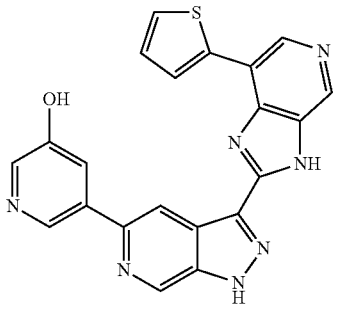
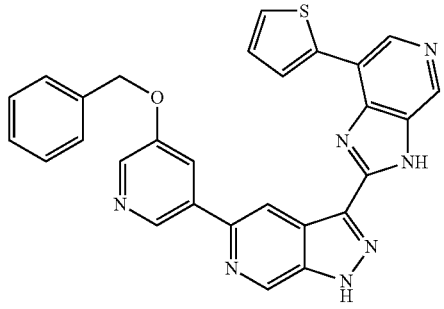
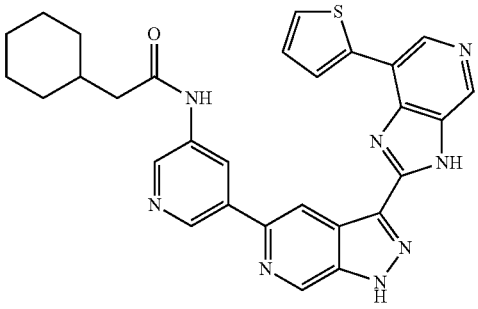
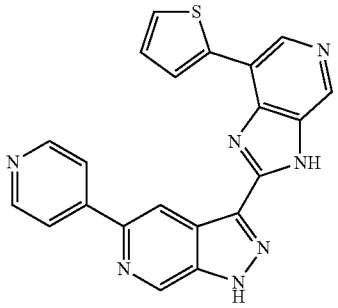
1094	
1095	
1096	
1097	
1098	

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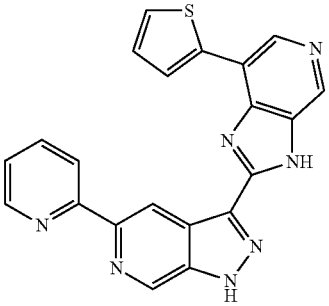
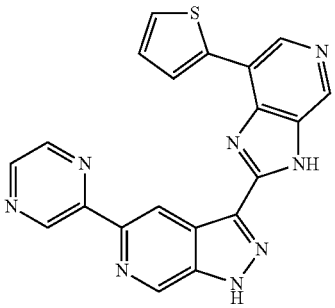
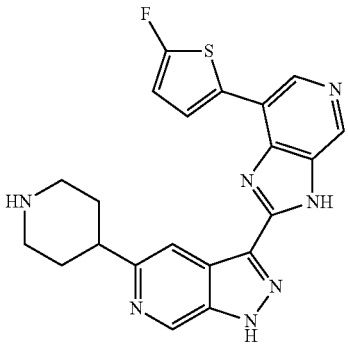
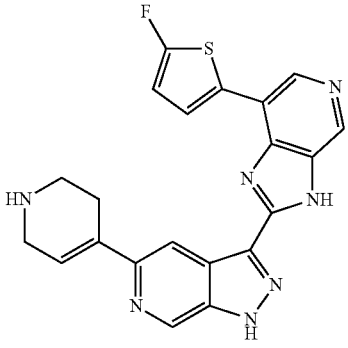
1099	
1100	
1101	
1102	

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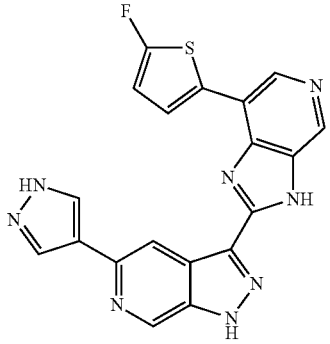
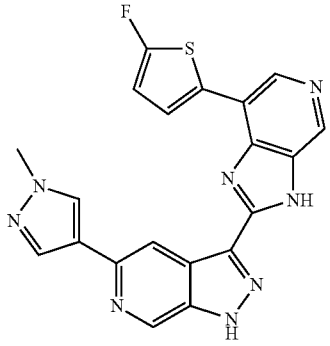
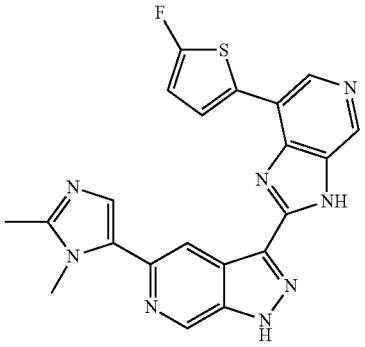
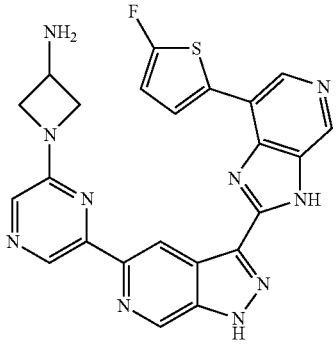
1103	
1104	
1105	
1106	

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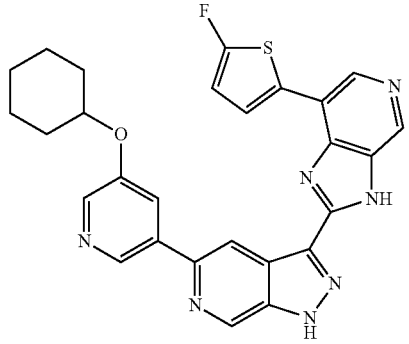
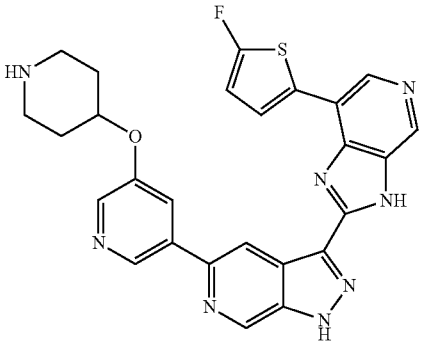
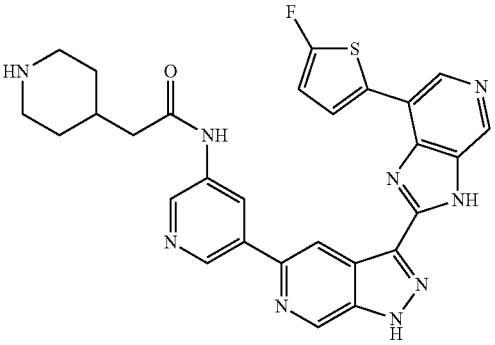
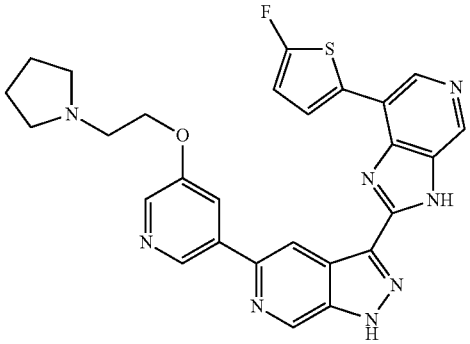
1107	
1108	
1109	
1110	

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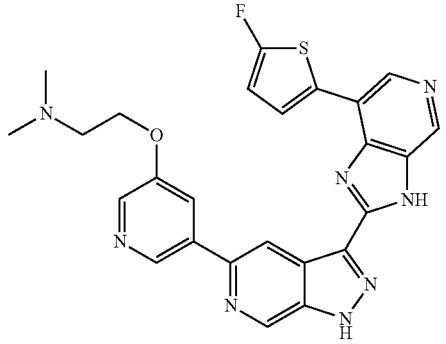
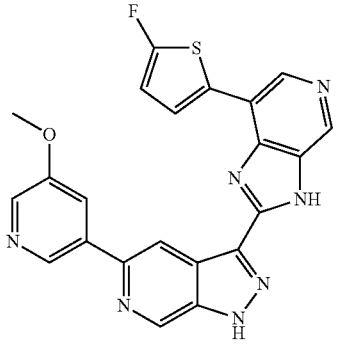
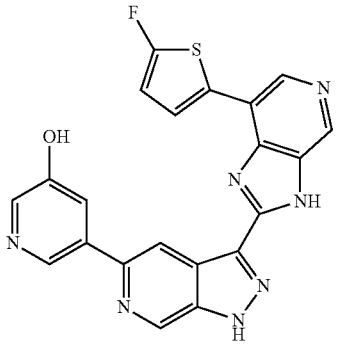
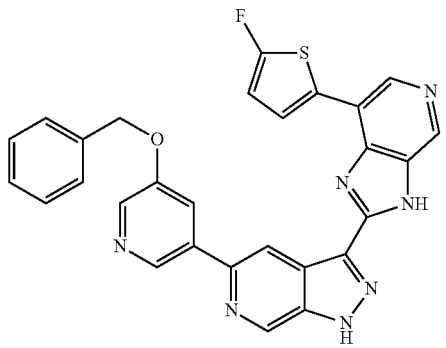
1111	
1112	
1113	
1114	

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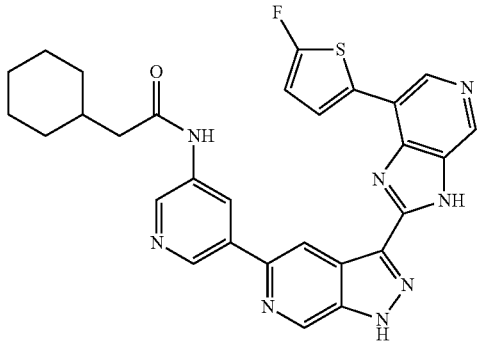
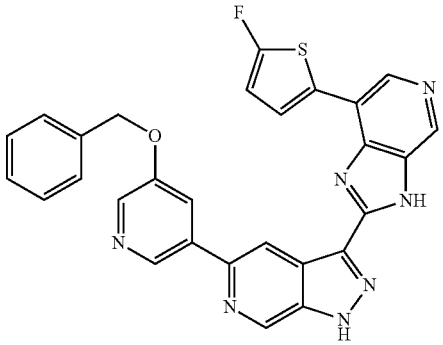
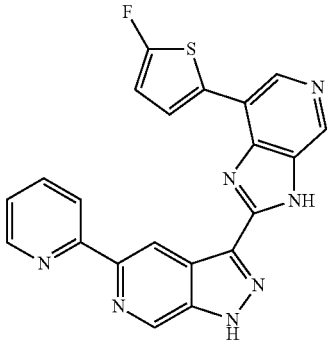
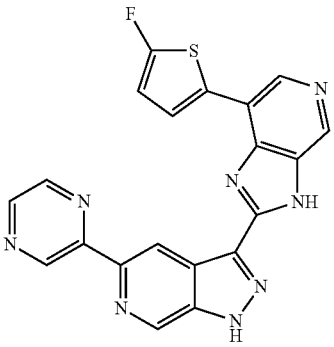
1115	
1116	
1117	
1118	

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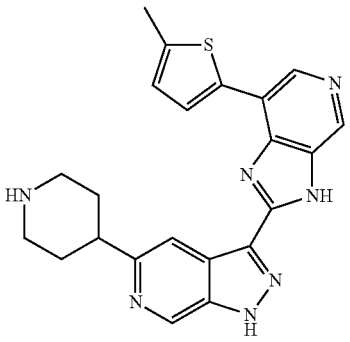
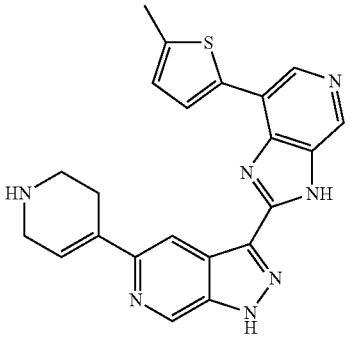
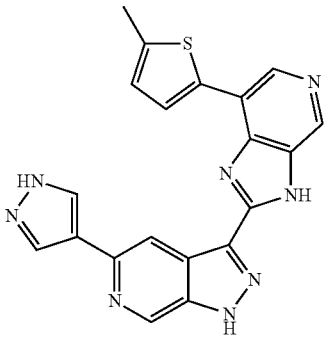
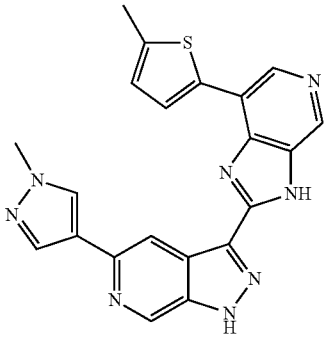
1119	
1120	
1121	
1122	

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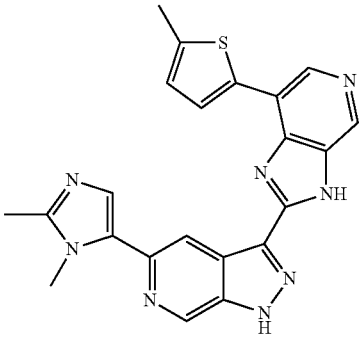
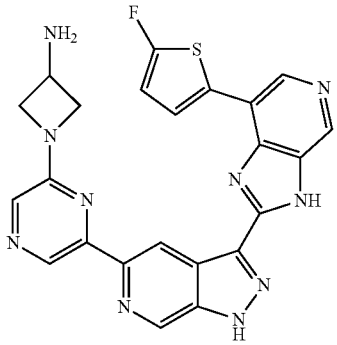
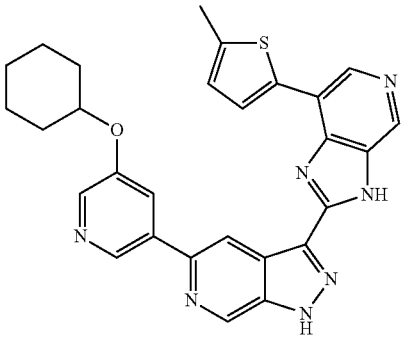
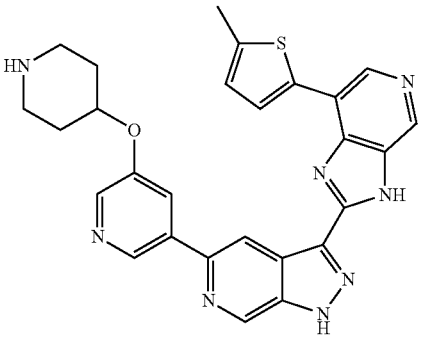
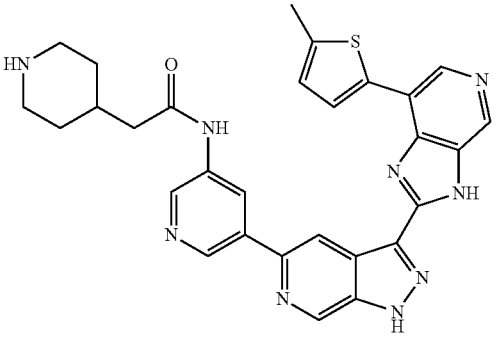
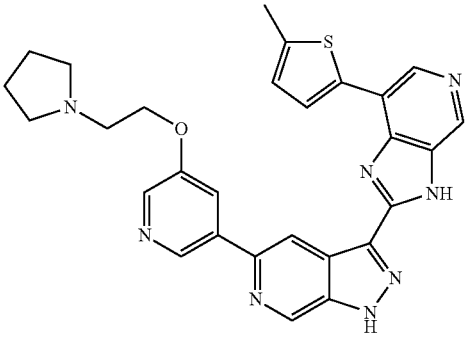
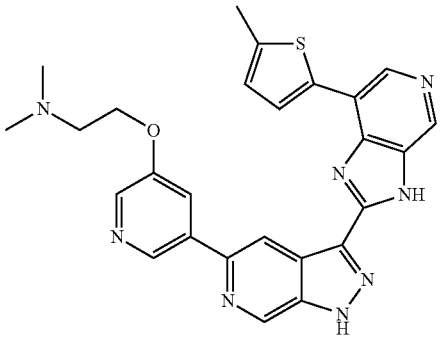
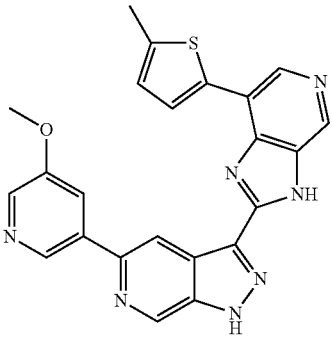
1123	
1124	
1125	
1126	

TABLE 1-continued

1127	
1128	
1129	
1130	

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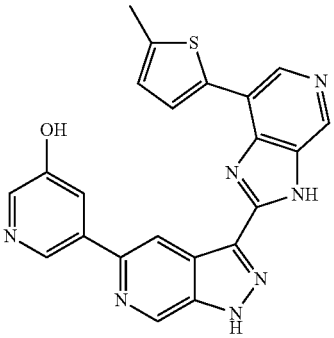
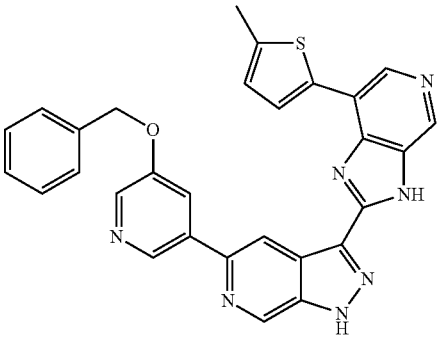
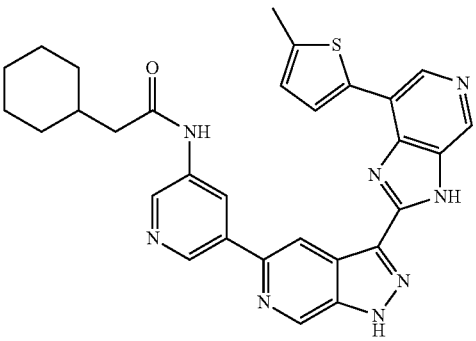
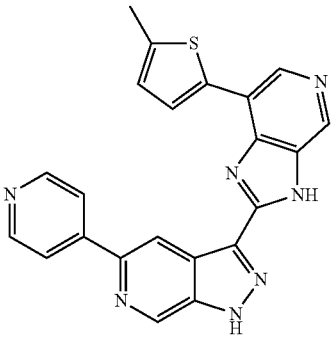
1131	
1132	
1133	
1134	

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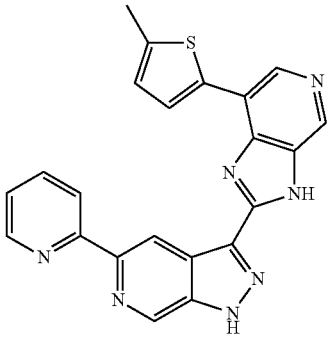
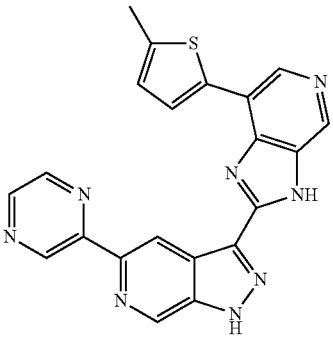
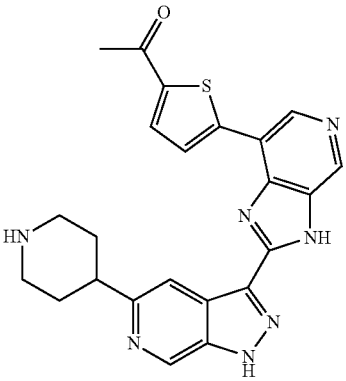
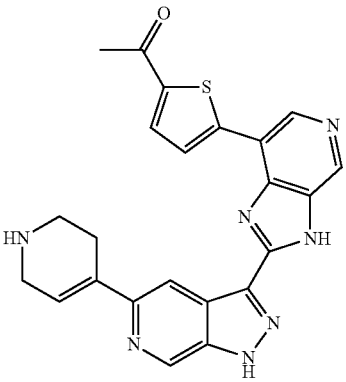
1135	
1136	
1137	
1138	

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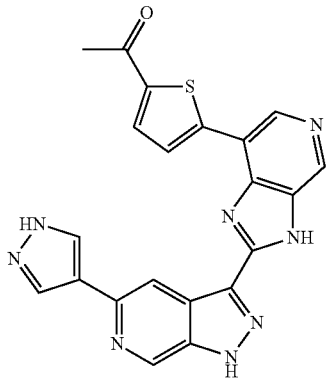
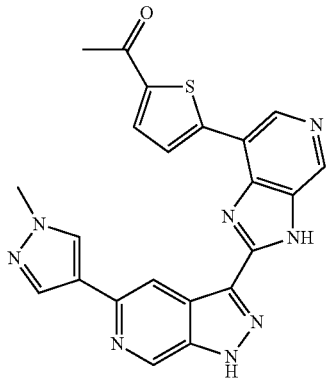
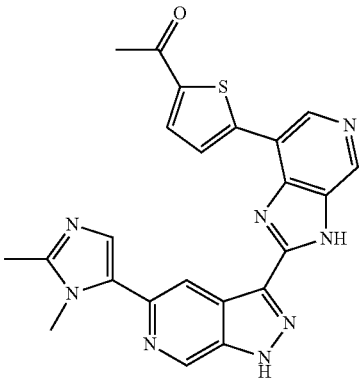
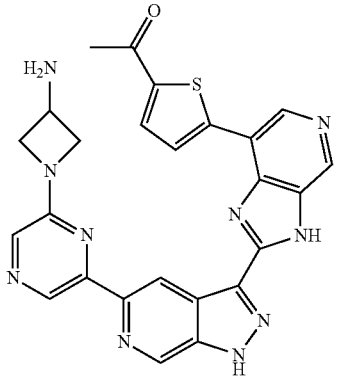
1139	
1140	
1141	
1142	

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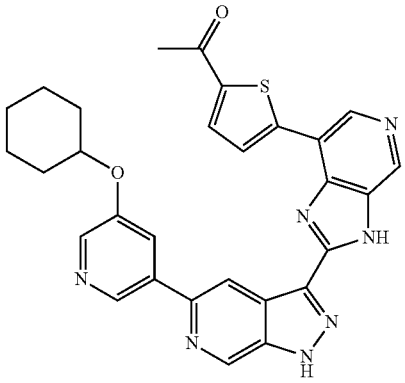
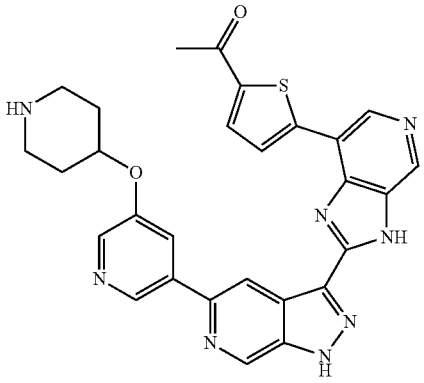
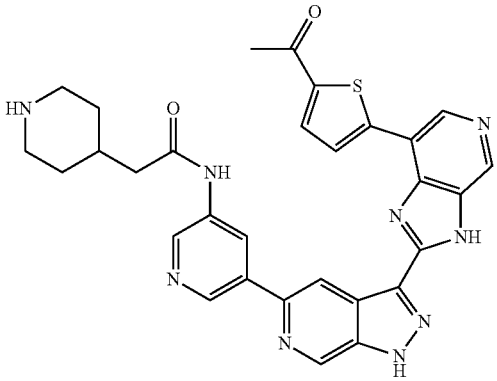
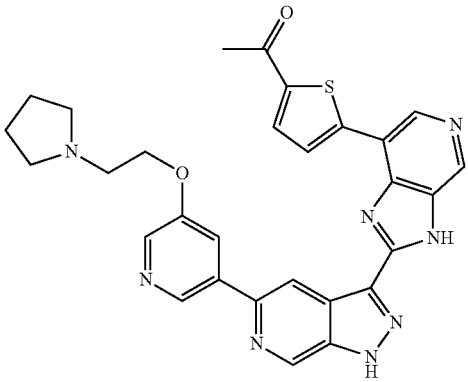
1143	
1144	
1145	
1146	

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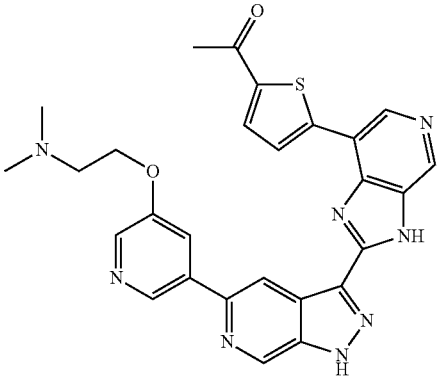
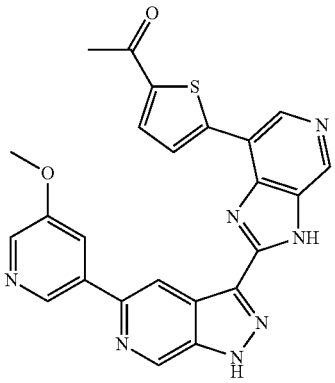
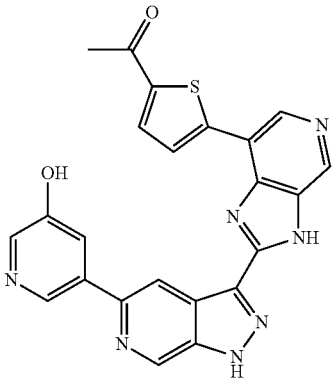
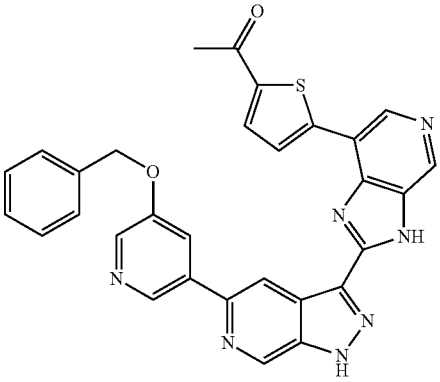
1147	
1148	
1149	
1150	

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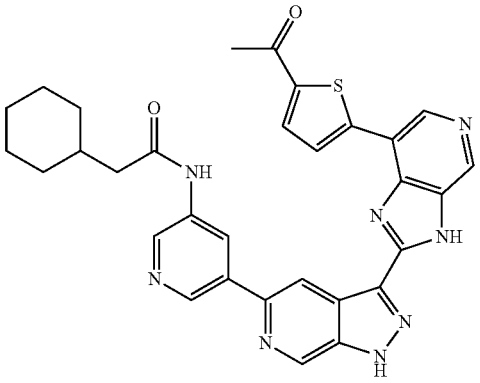
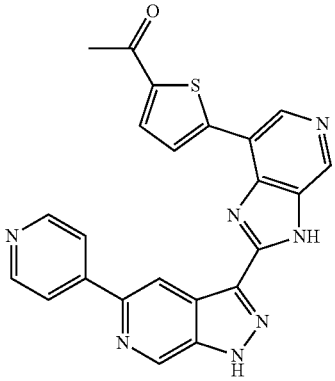
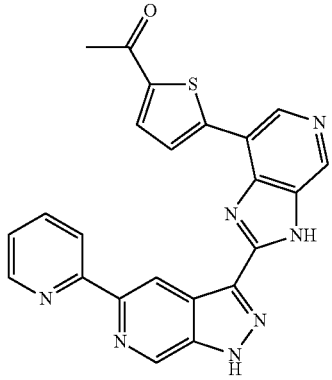
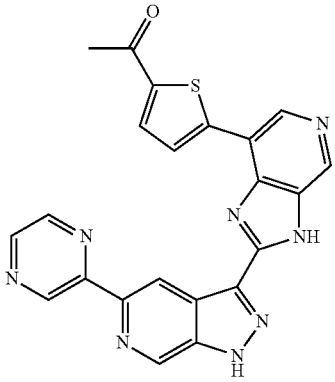
1151	
1152	
1153	
1154	

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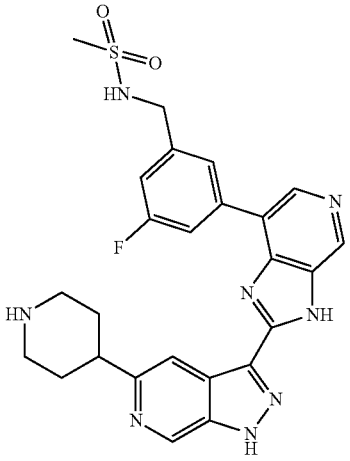
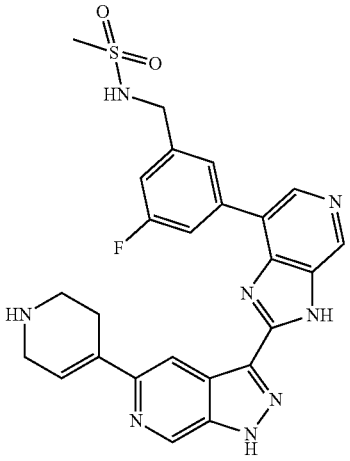
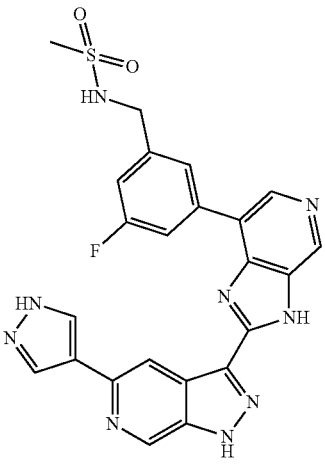
1155	
1156	
1157	

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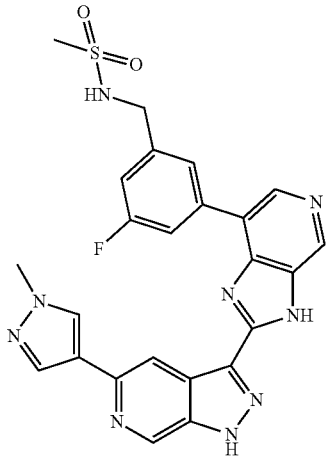
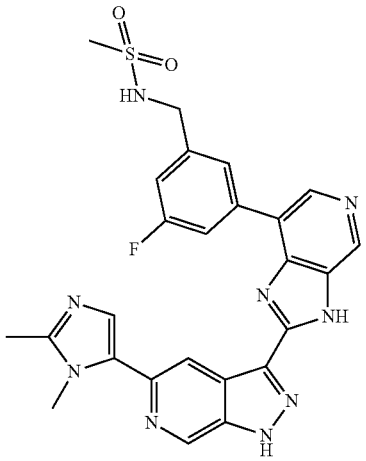
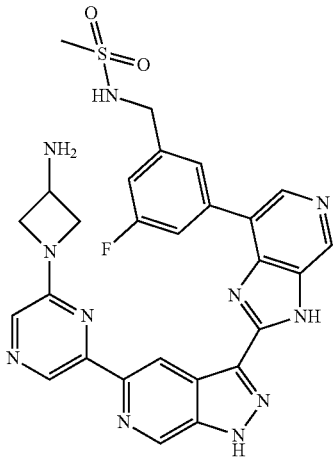
1158	
1159	
1160	

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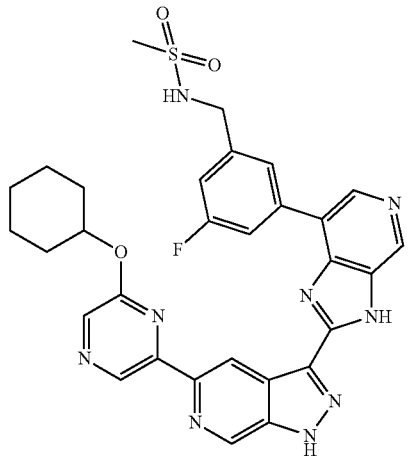
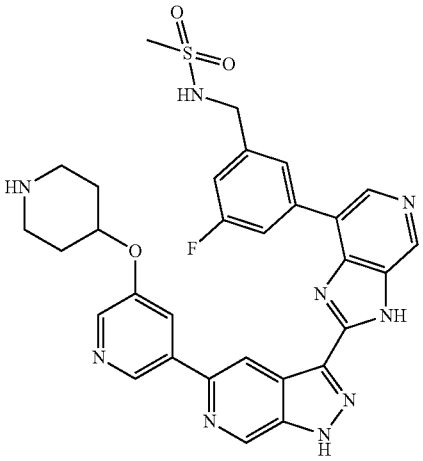
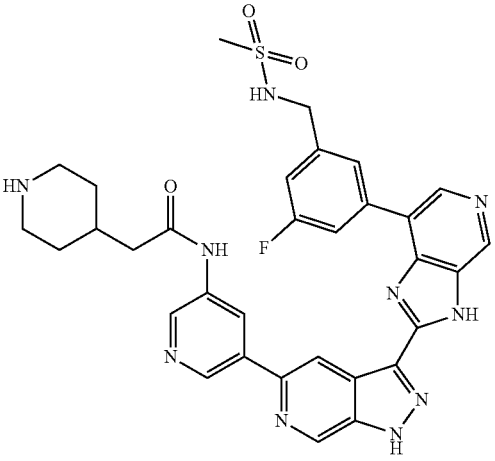
1161	
1162	
1163	

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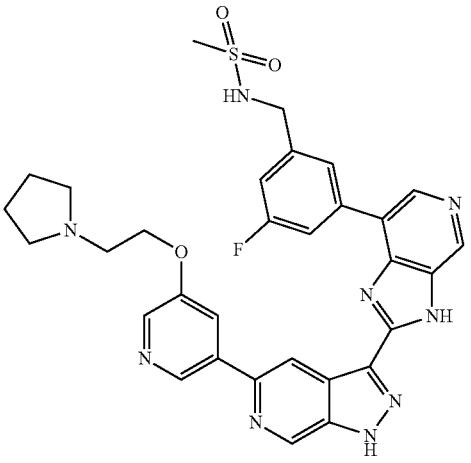
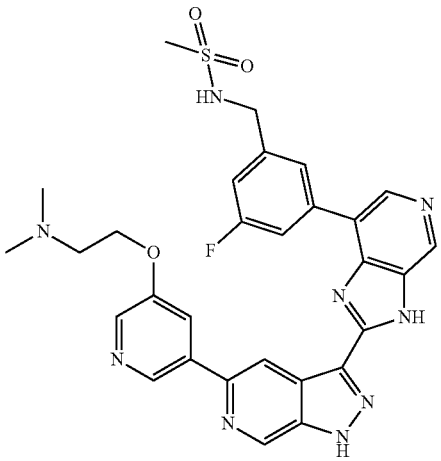
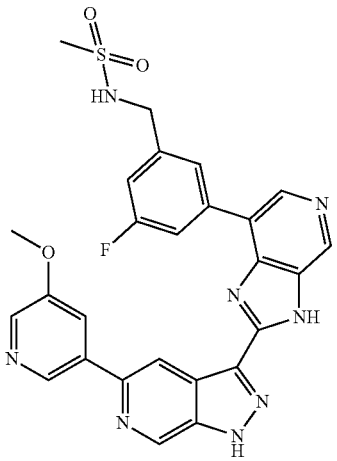
1164	
1165	
1166	

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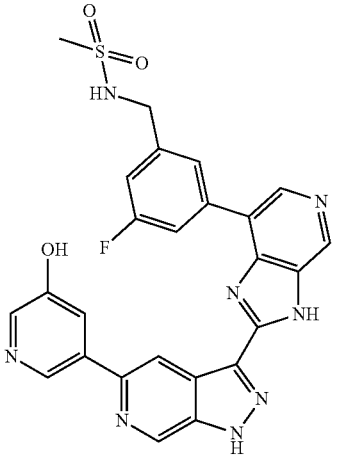
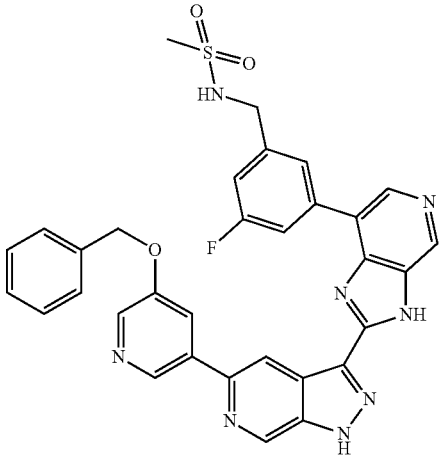
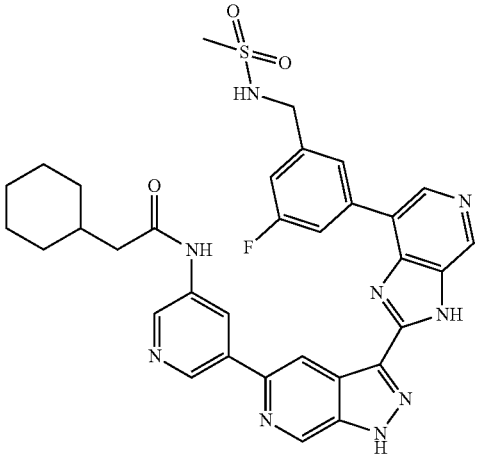
1167	
1168	
1169	

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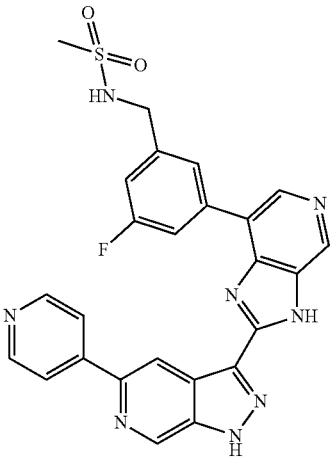
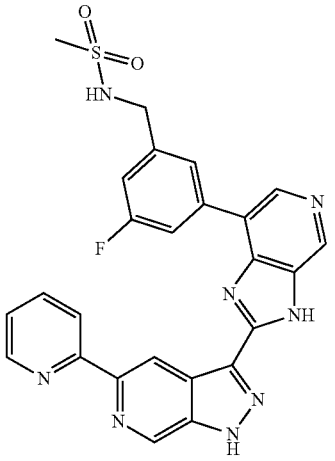
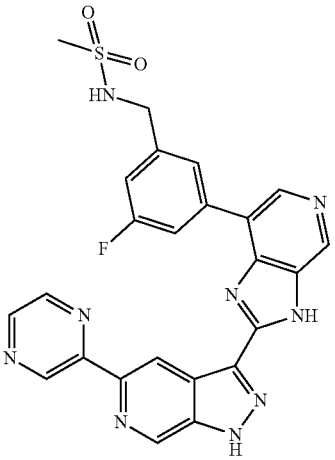
1170	
1171	
1172	

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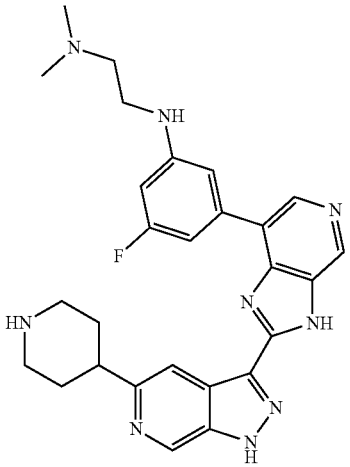
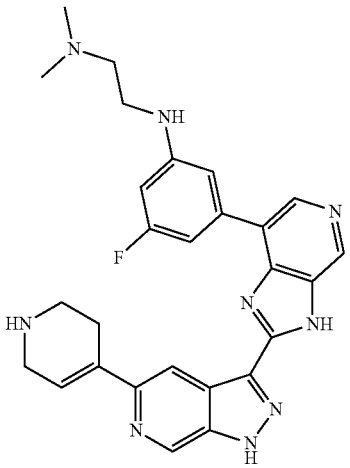
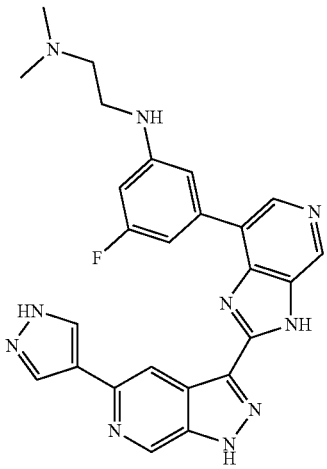
1173	
1174	
1175	

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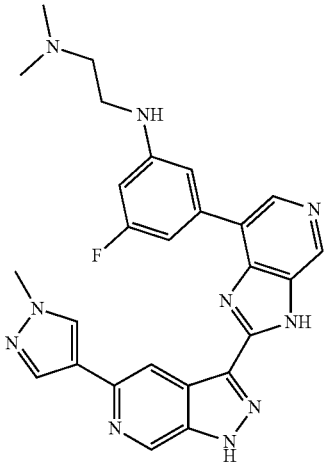
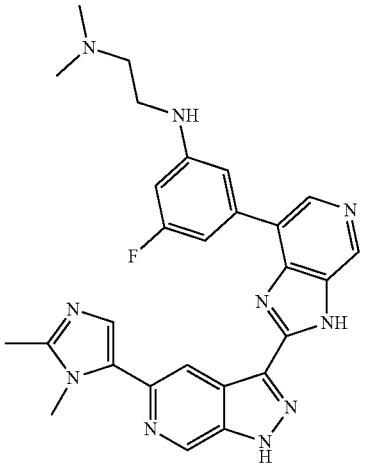
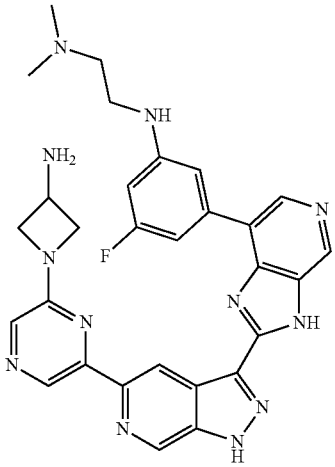
1176	
1177	
1178	

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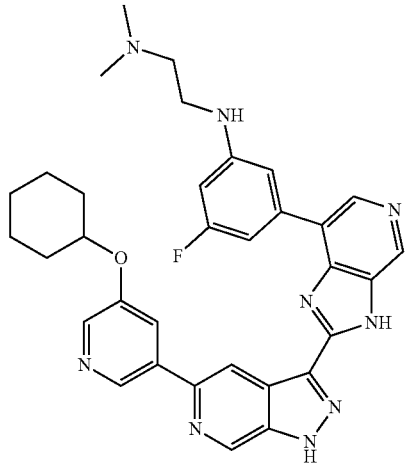
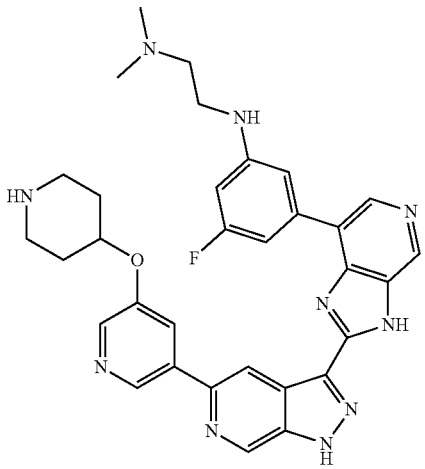
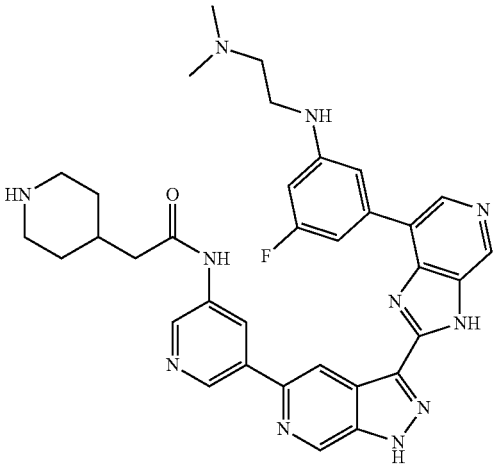
1179	
1180	
1181	

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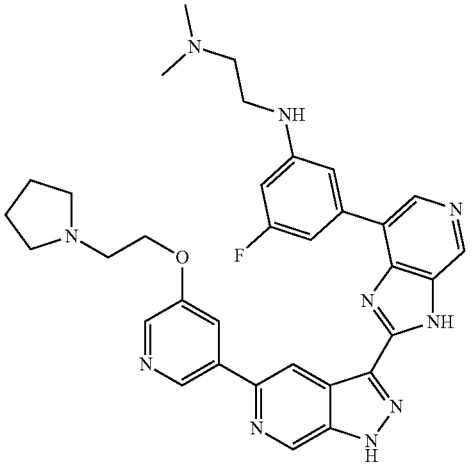
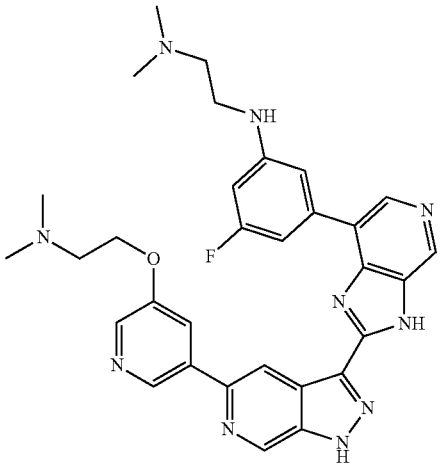
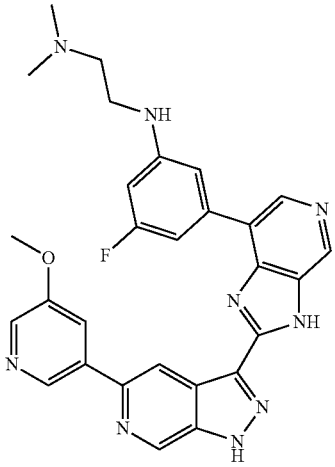
1182	
1183	
1184	

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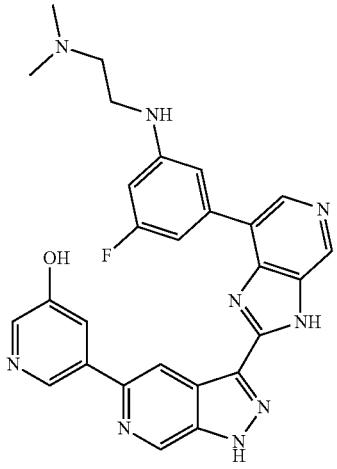
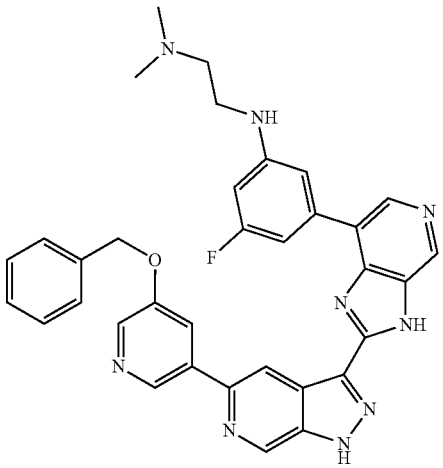
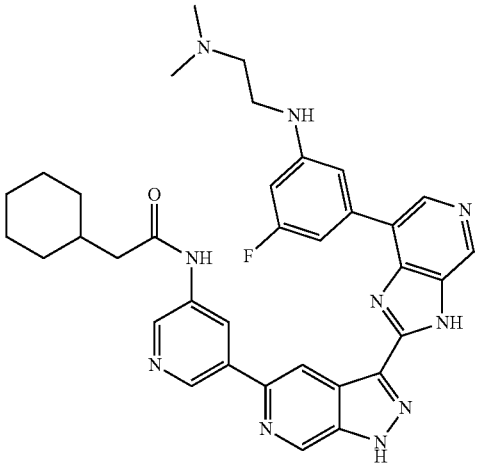
1185	
1186	
1187	

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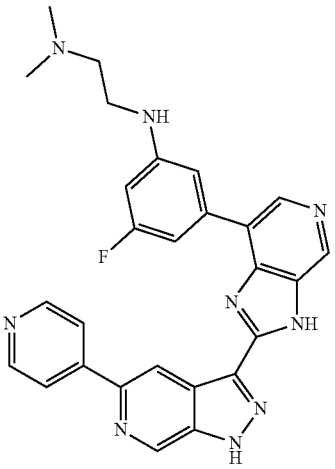
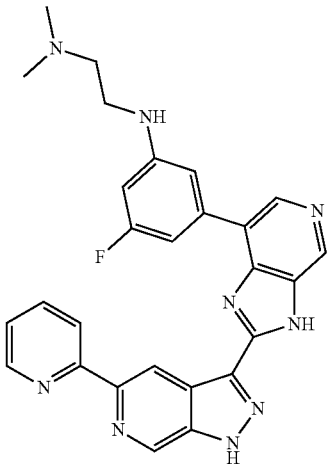
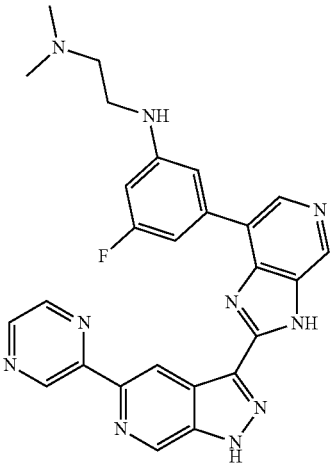
1188	
1189	
1190	

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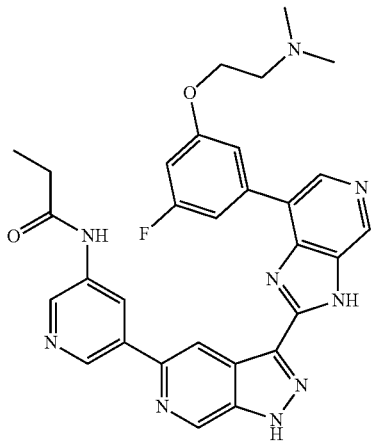
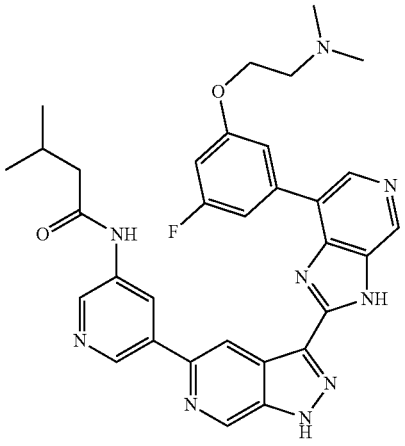
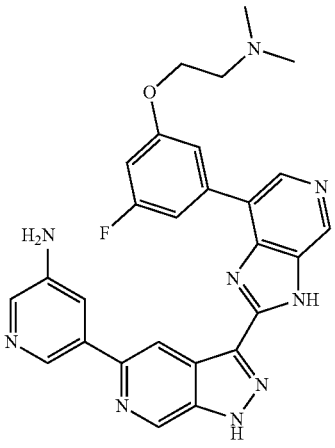
1191	
1192	
1193	

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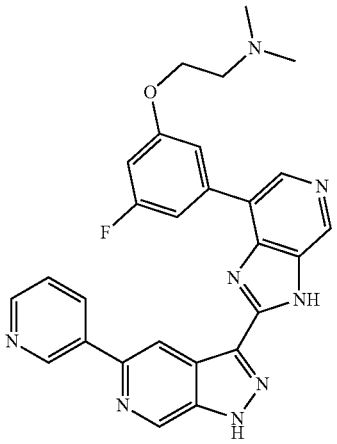
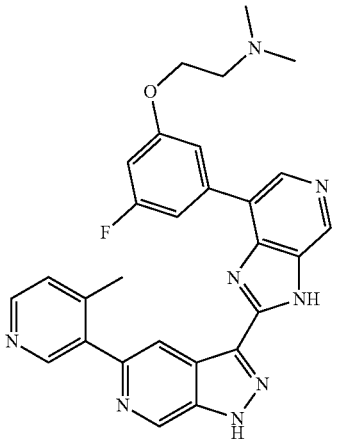
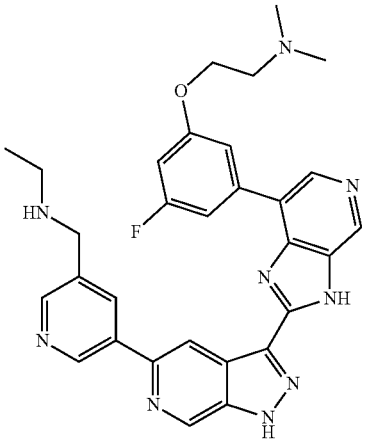
1194	
1195	
1196	

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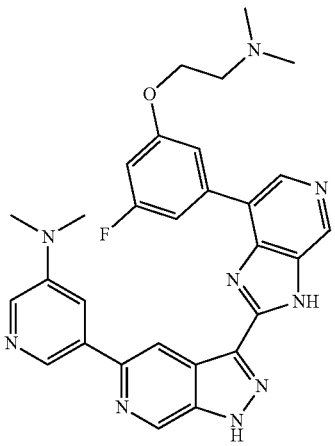
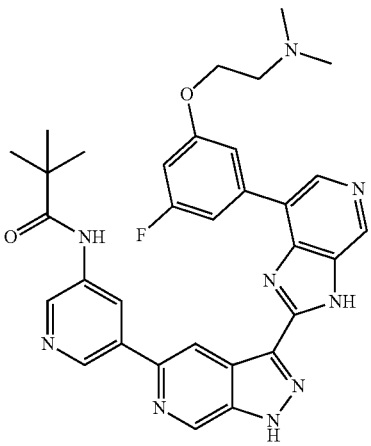
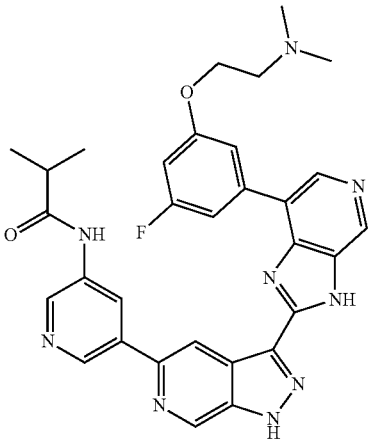
1197	
1198	
1199	

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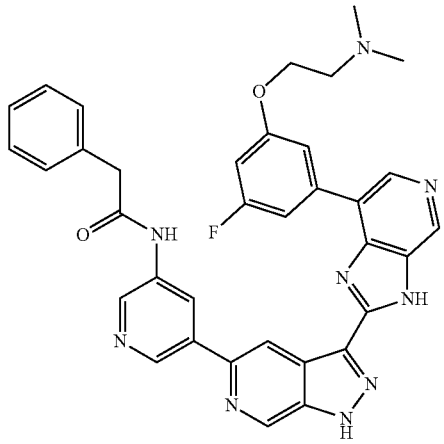
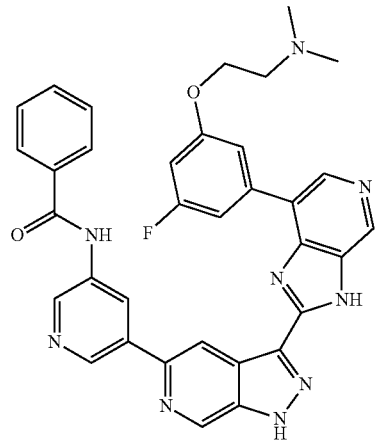
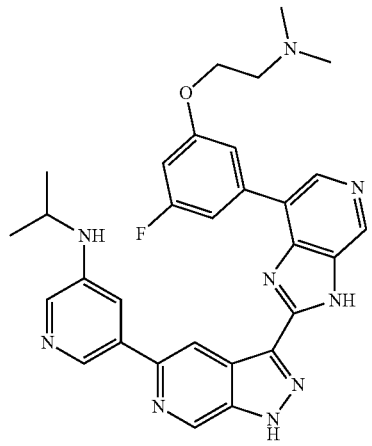
1200	
1201	
1202	

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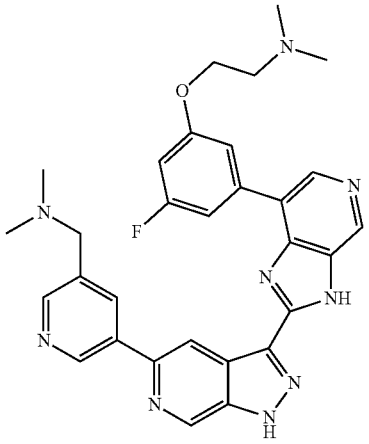
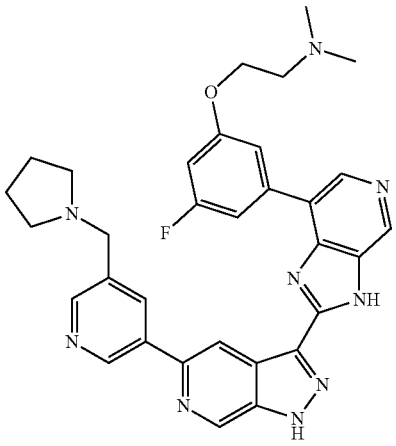
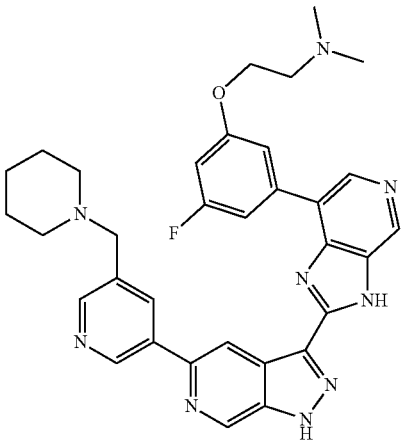
1203	
1204	
1205	

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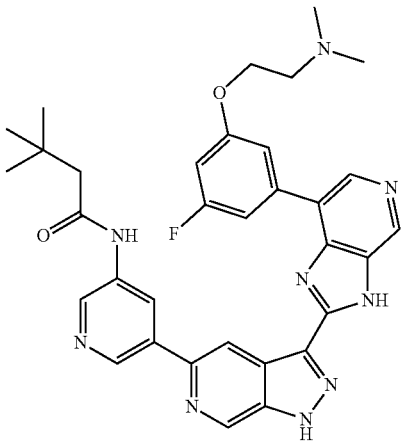
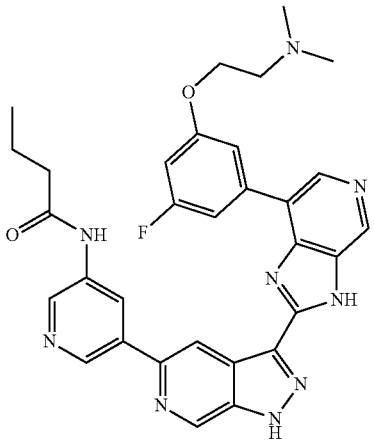
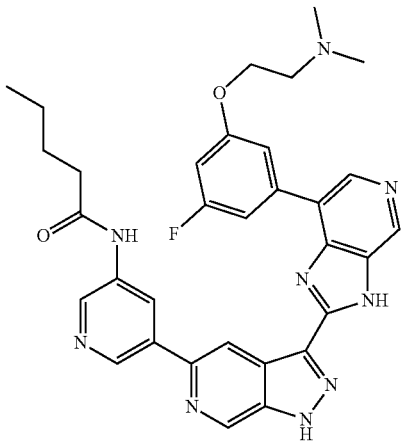
1206	
1207	
1208	

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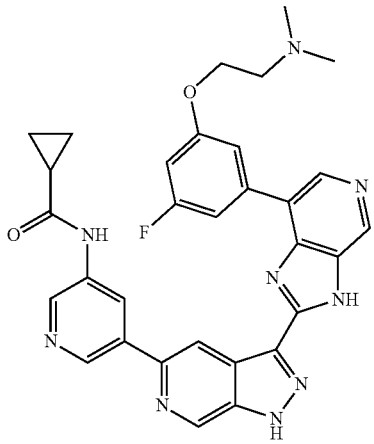
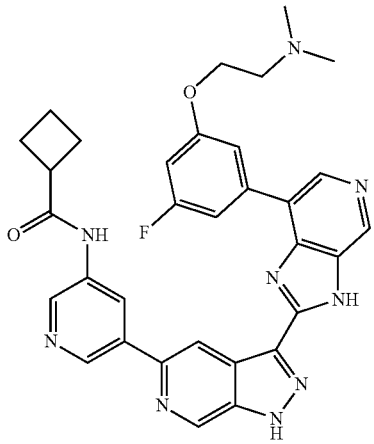
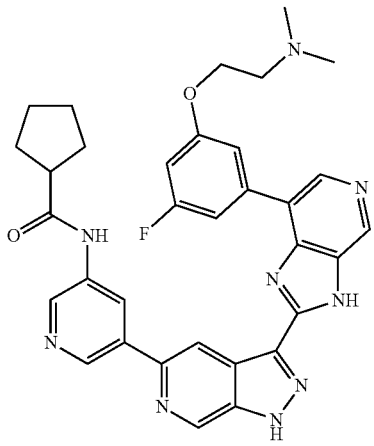
1209	
1210	
1211	

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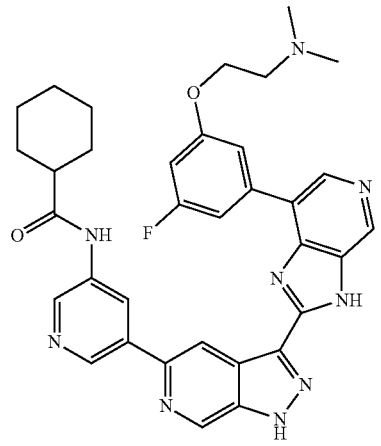
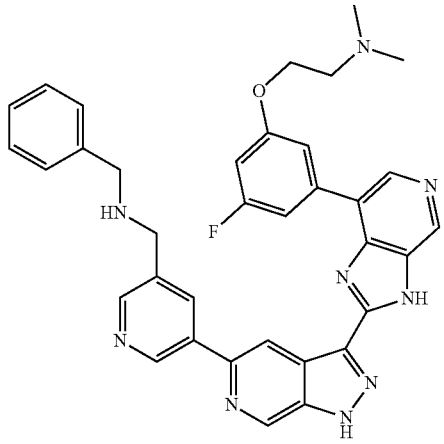
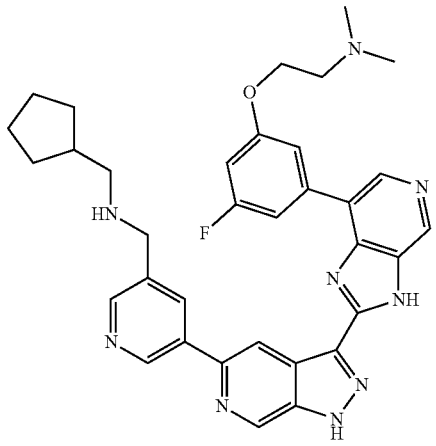
1212	
1213	
1214	

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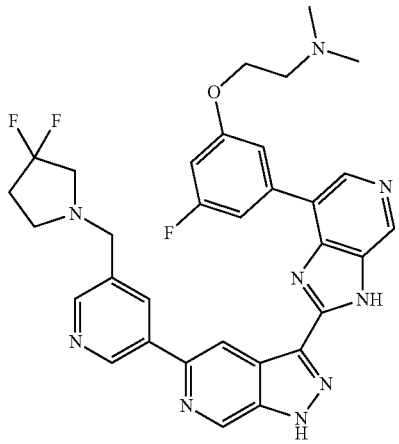
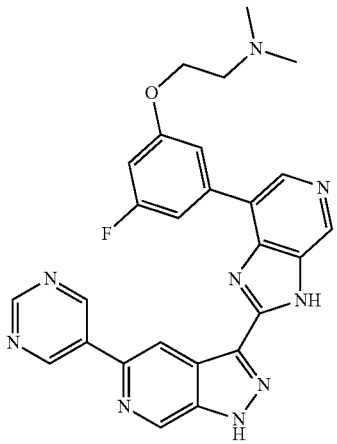
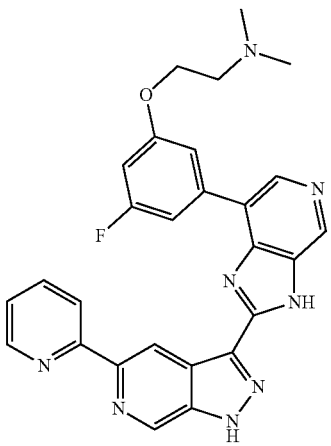
1215	
1216	
1217	

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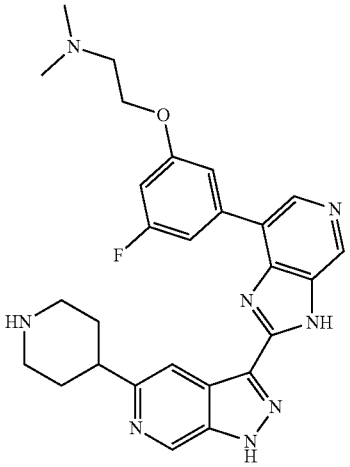

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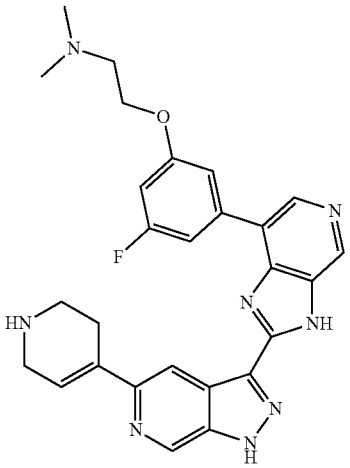

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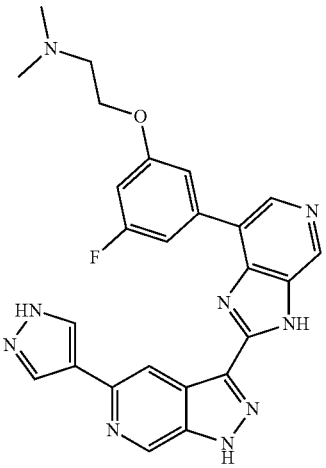

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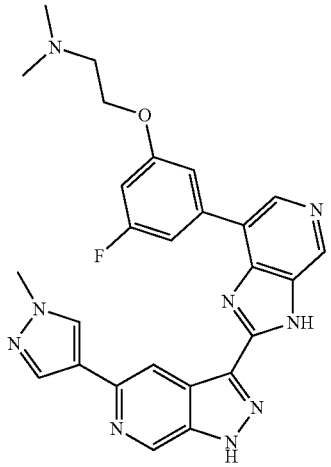

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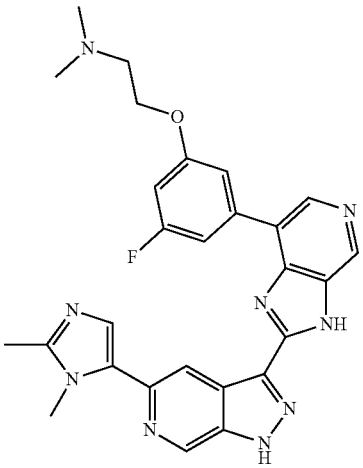

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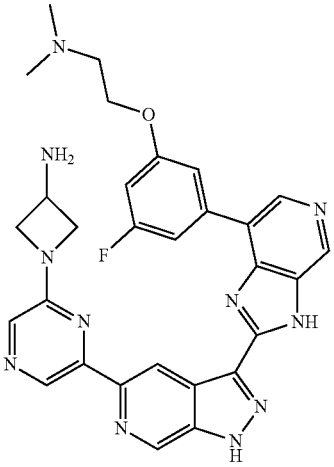

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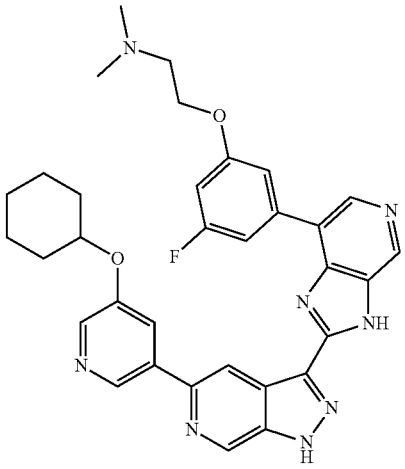
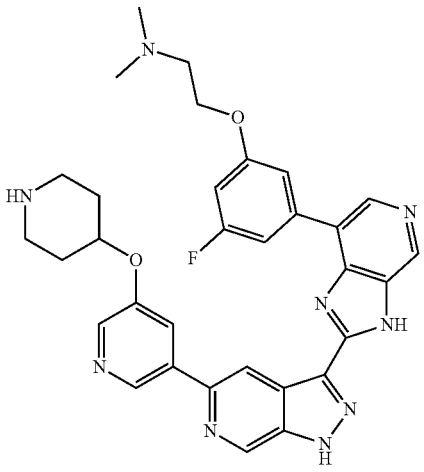
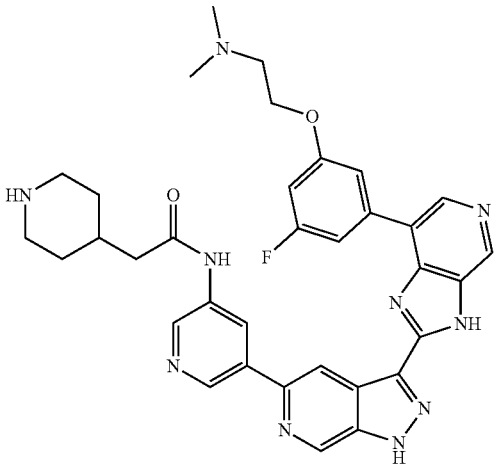
1224	
1225	
1226	

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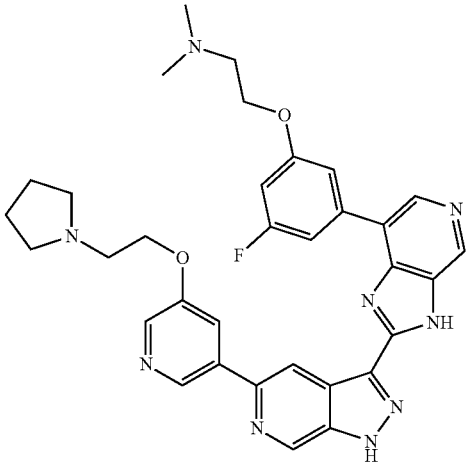
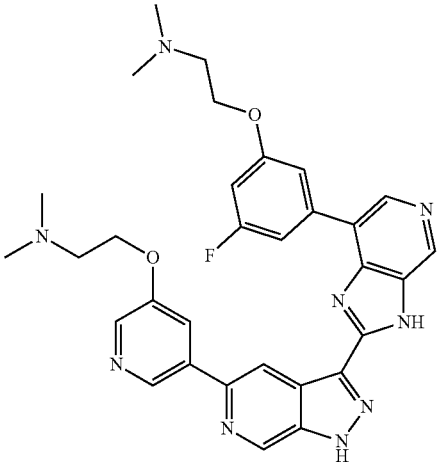
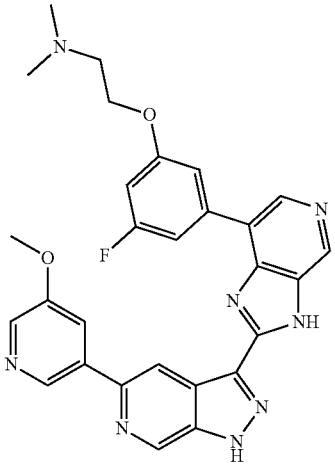
1227	
1228	
1229	

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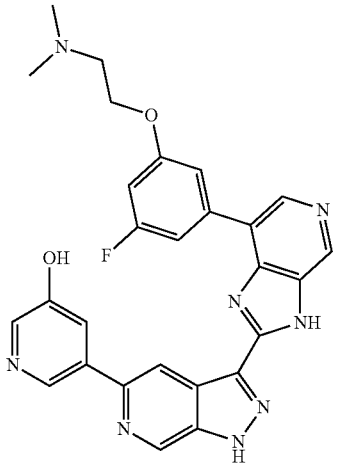
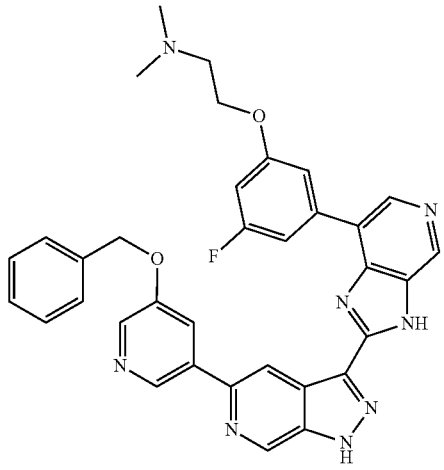
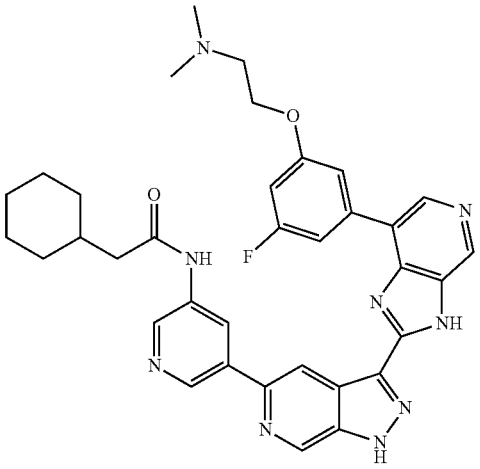
1230	
1231	
1232	

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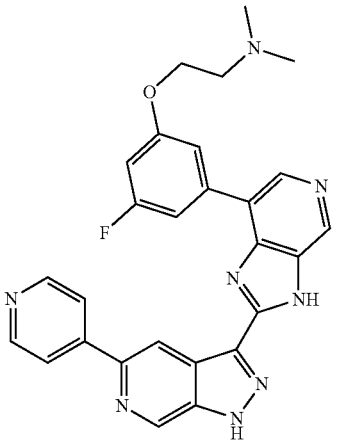
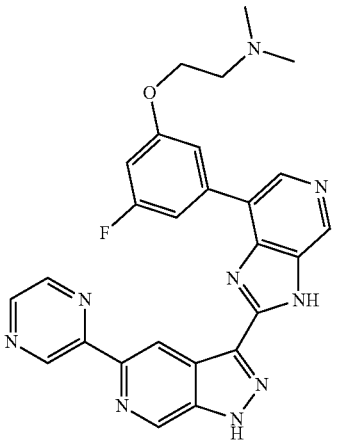
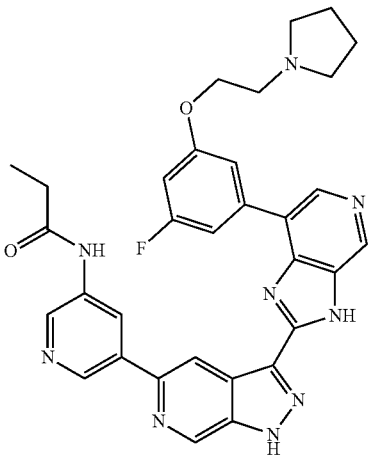
1233	
1234	
1235	

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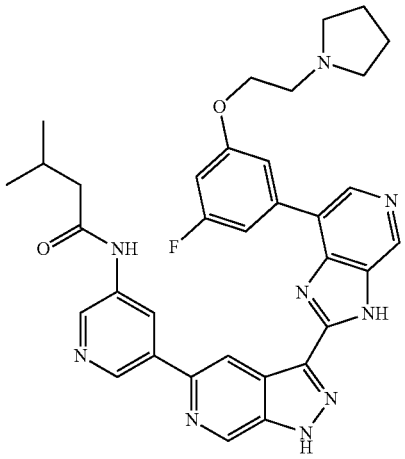
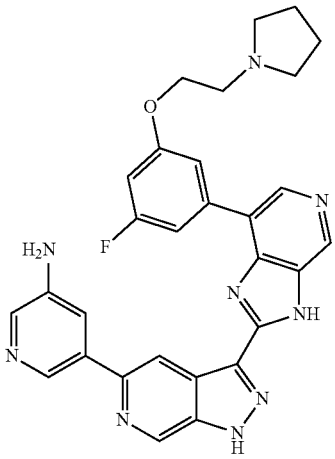
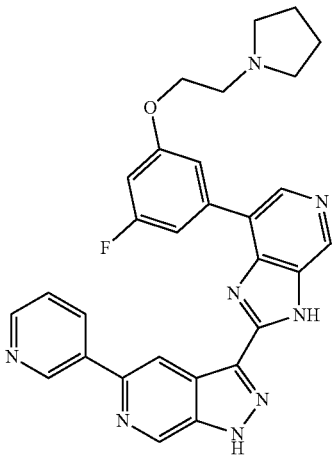
1236	
1237	
1238	

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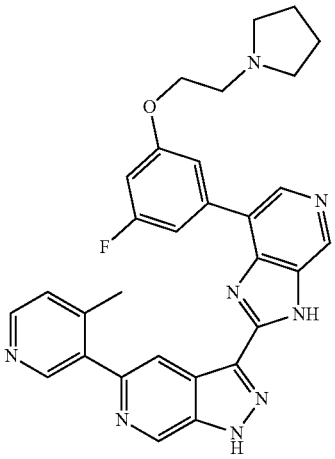
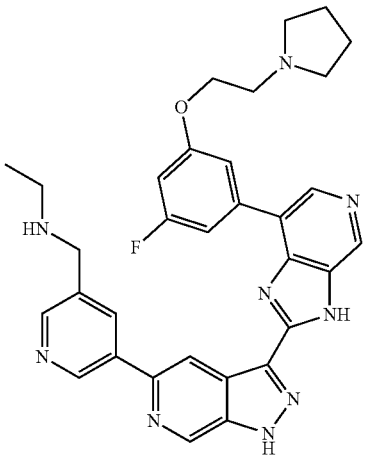
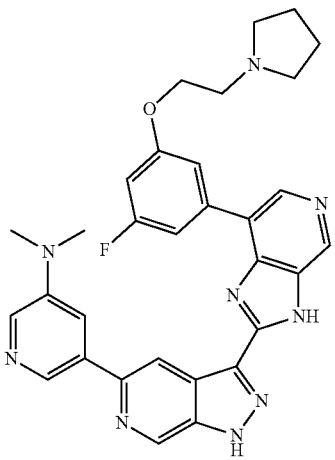
1239	
1240	
1241	

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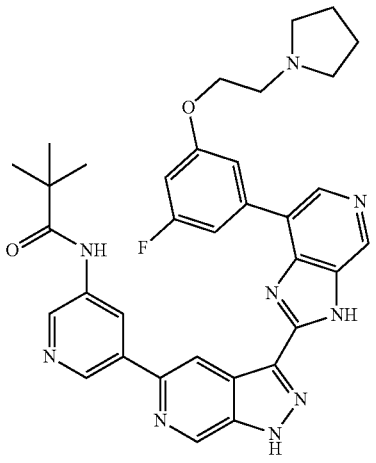
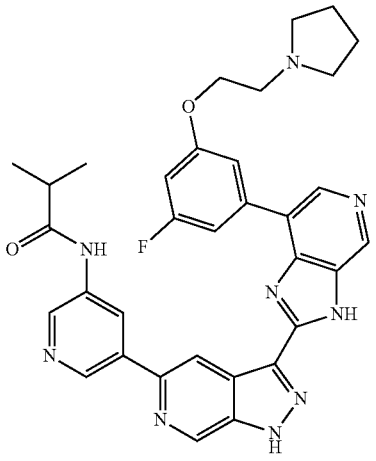
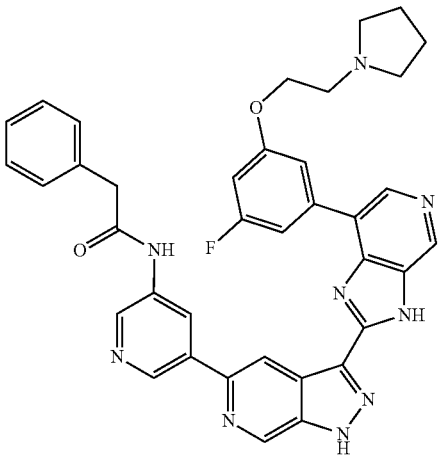
1242	
1243	
1244	

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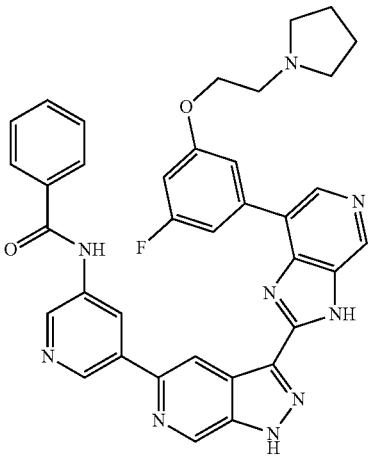
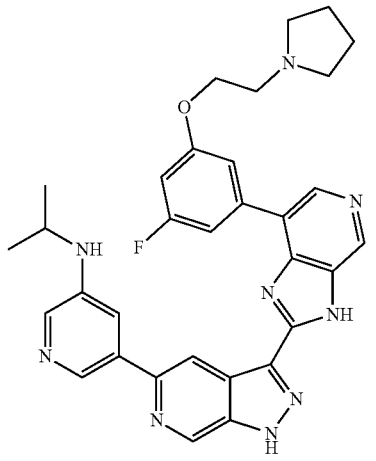
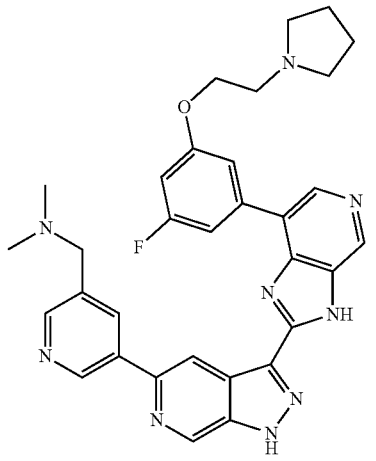
1245	
1246	
1247	

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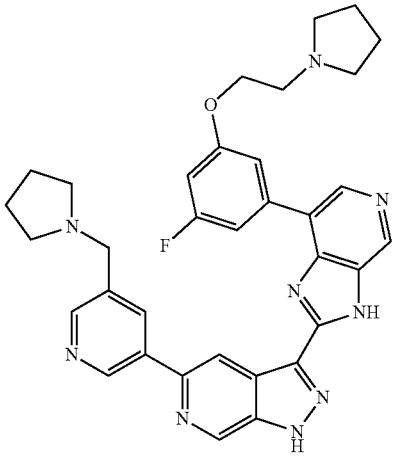
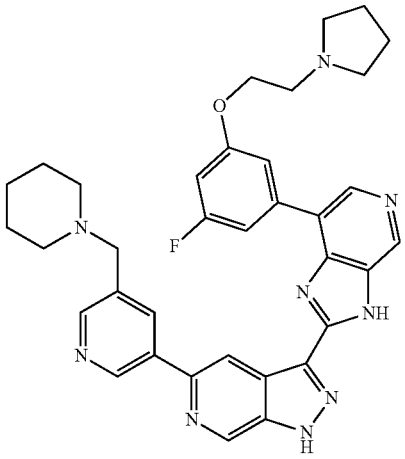
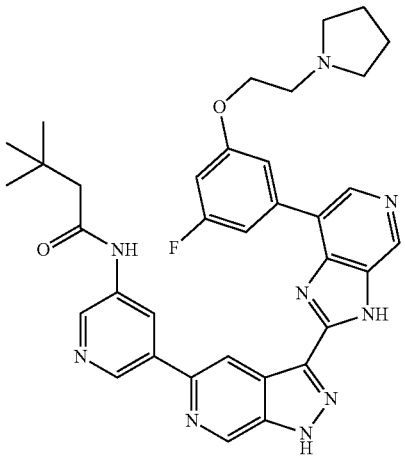
1248	
1249	
1250	

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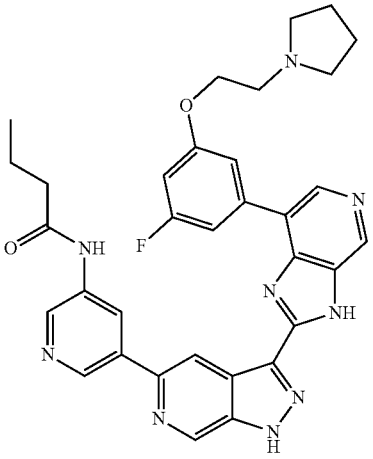
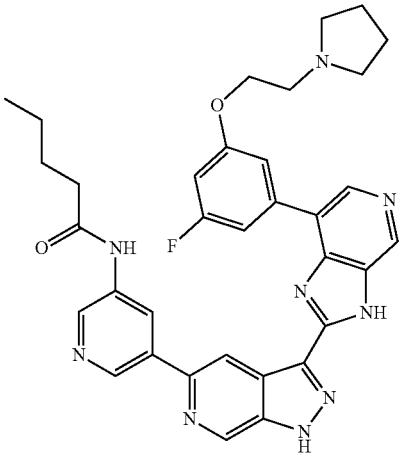
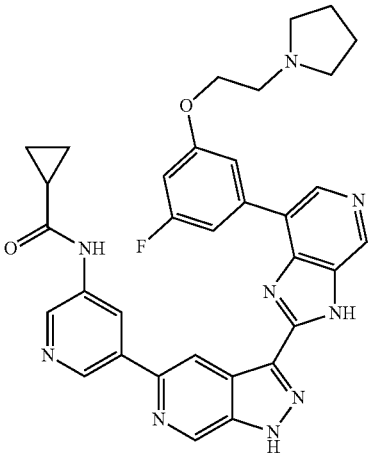
1251	
1252	
1253	

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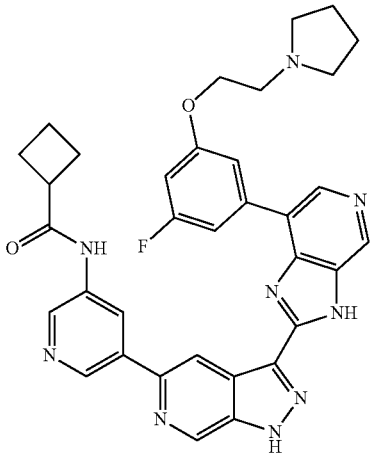
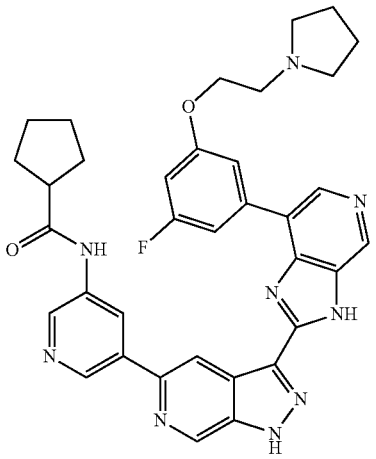
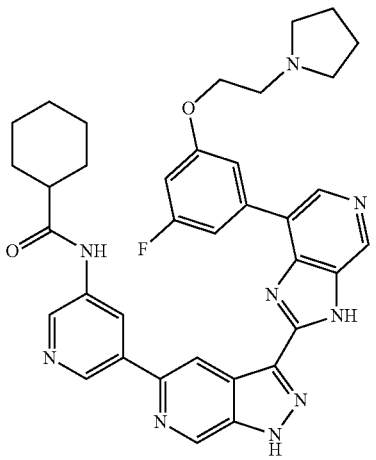
1254	
1255	
1256	

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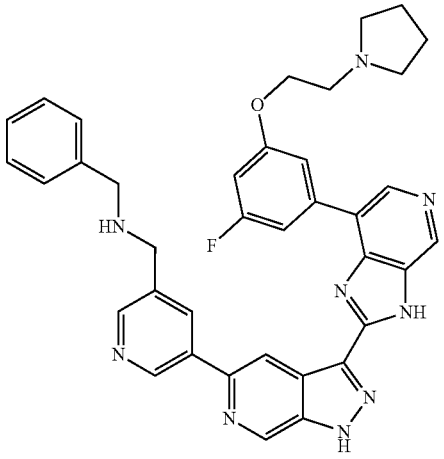
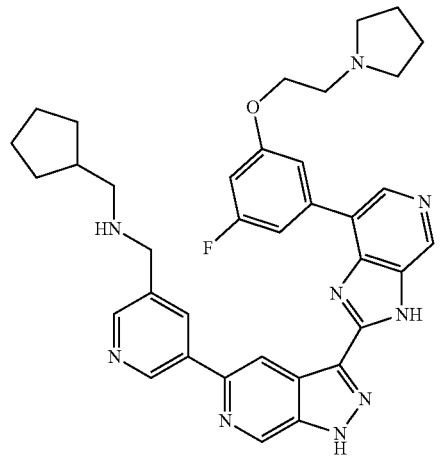
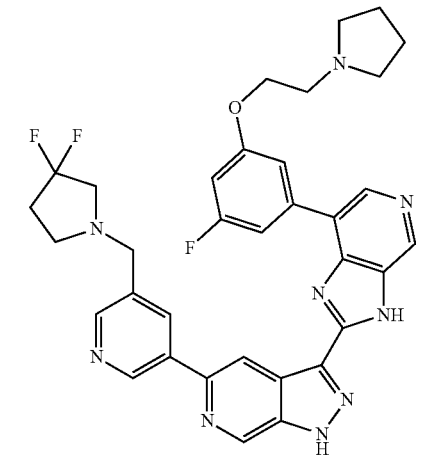
1257	
1258	
1259	

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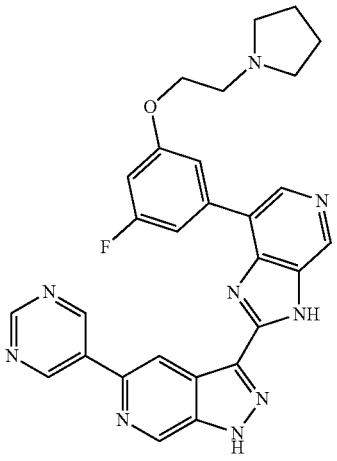
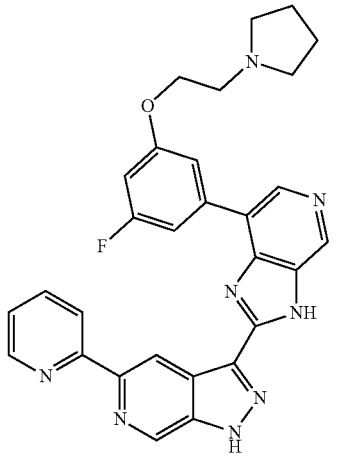
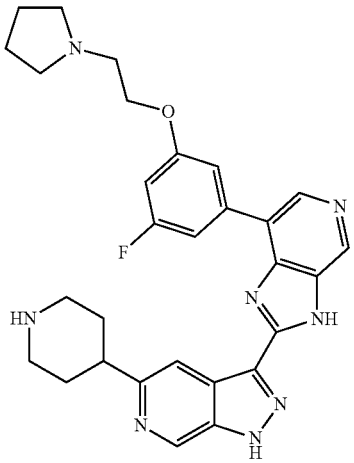
1260	
1261	
1262	

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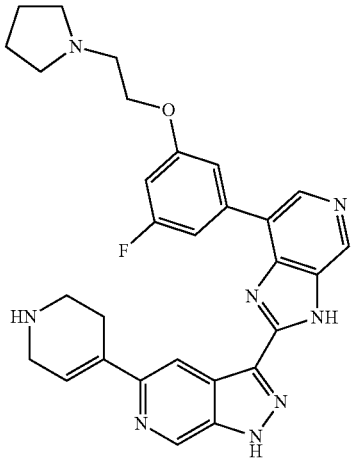
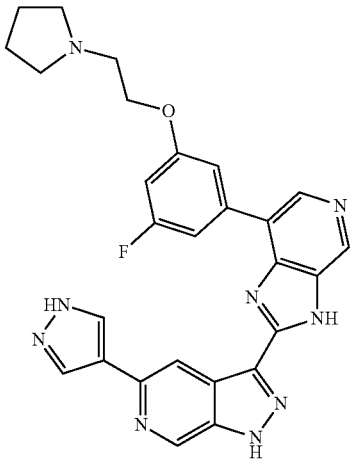
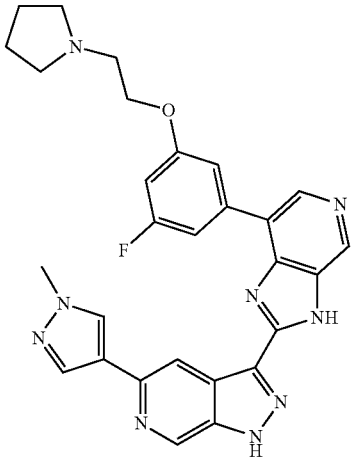
1263	
1264	
1265	

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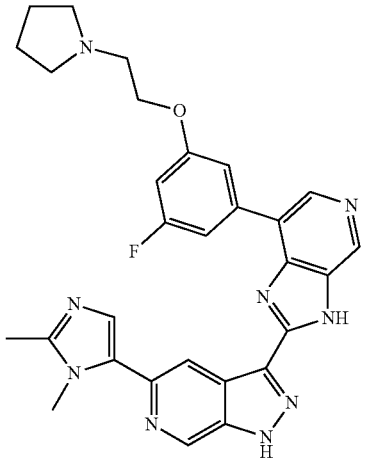
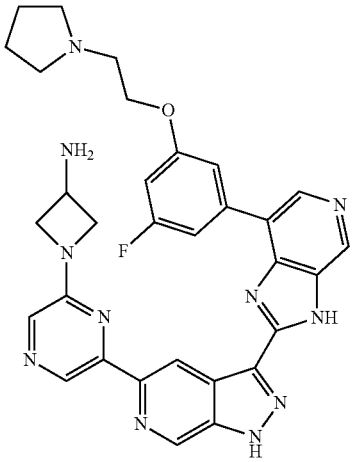
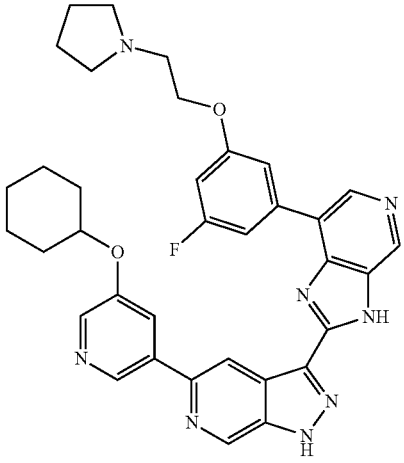
1266	
1267	
1268	

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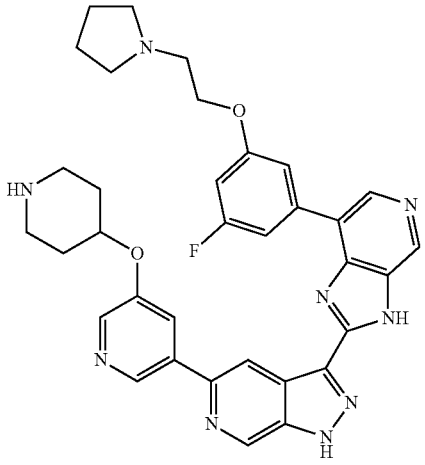
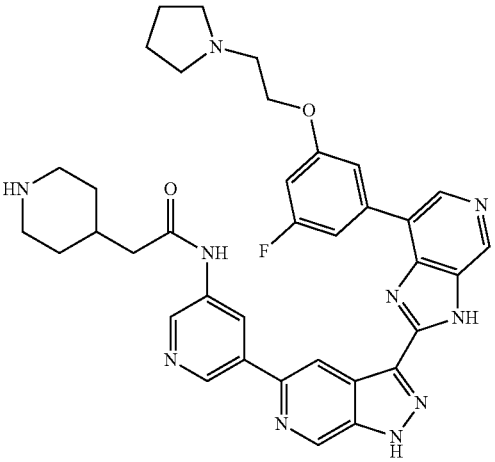
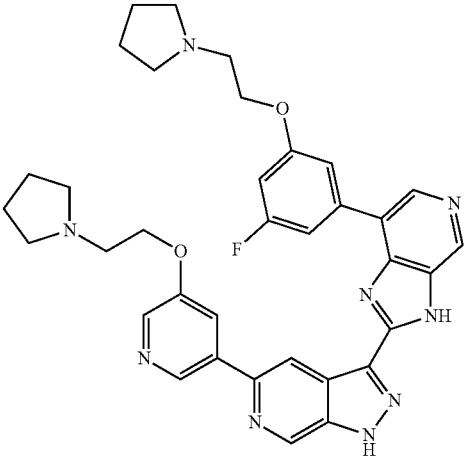
1269	
1270	
1271	

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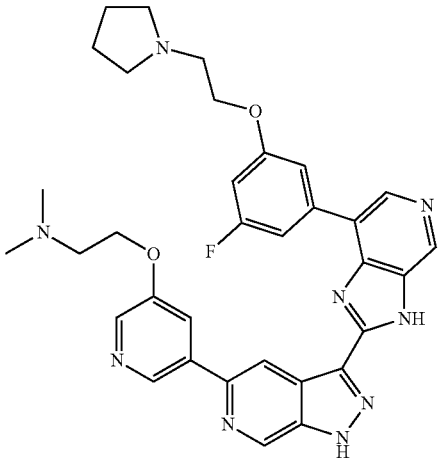
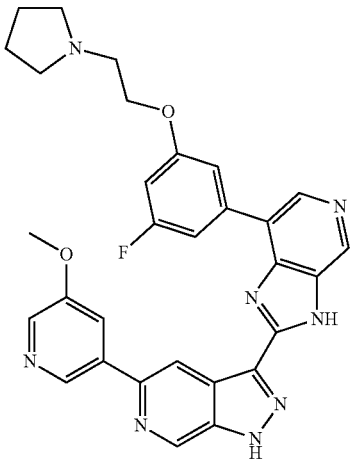
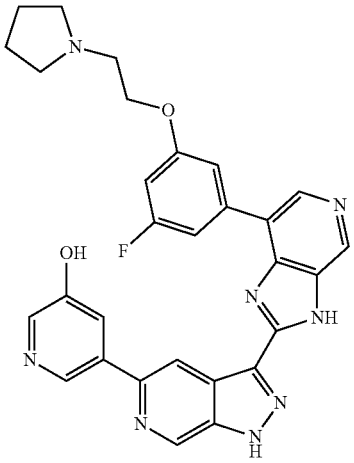
1272	
1273	
1274	

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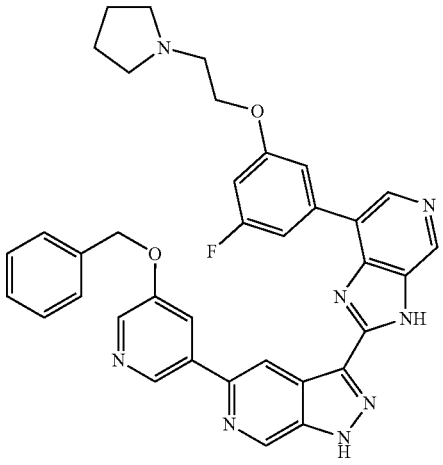
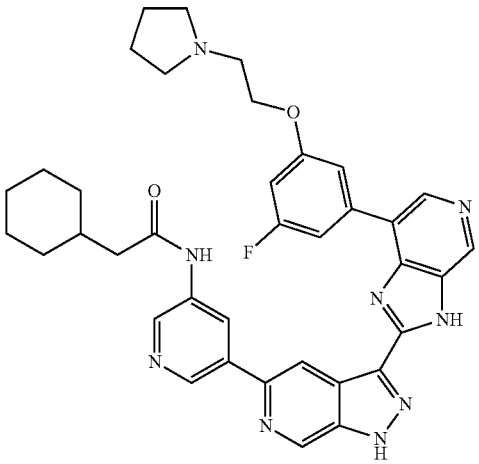
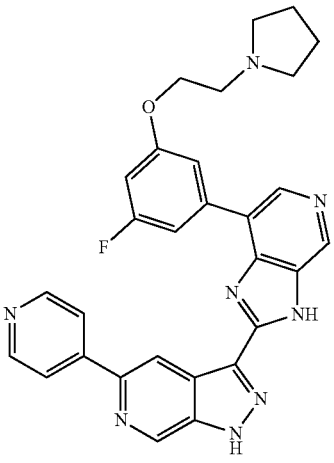
1275	
1276	
1277	

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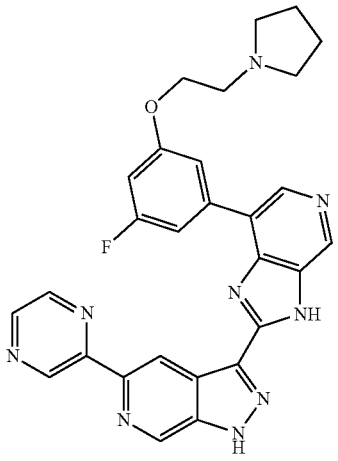
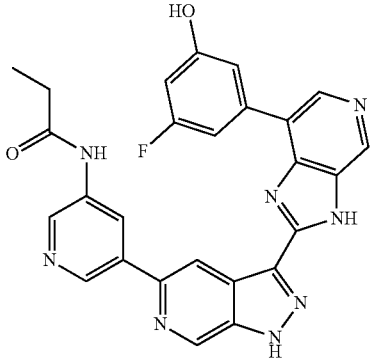
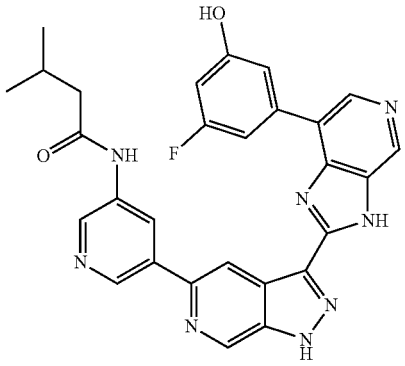
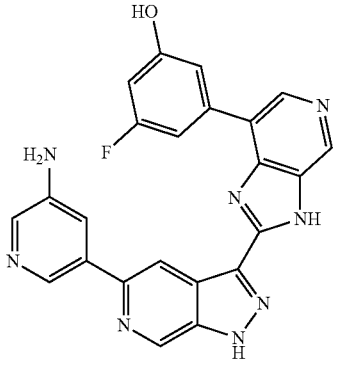
1278	
1279	
1280	
1281	

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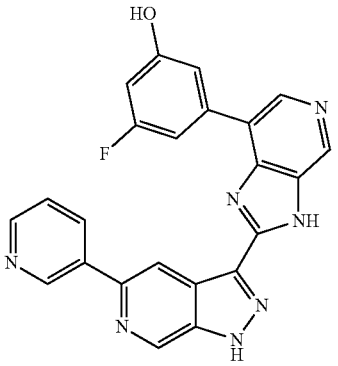
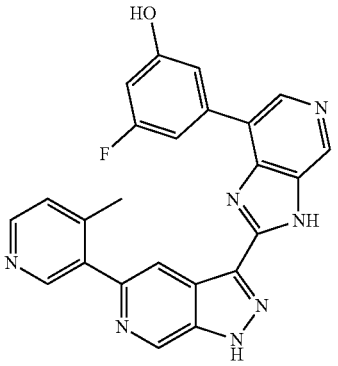
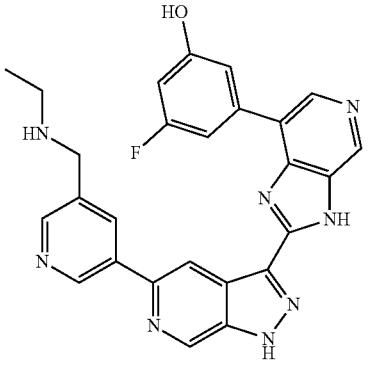
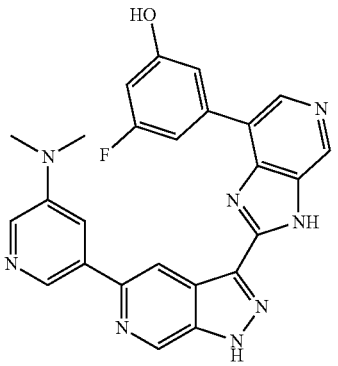
1282	
1283	
1284	
1285	

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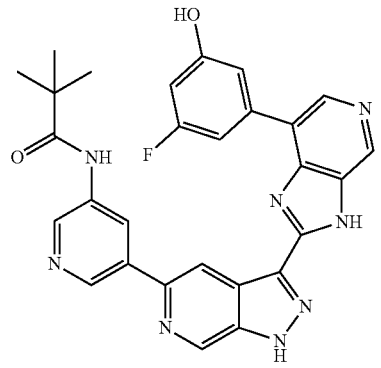
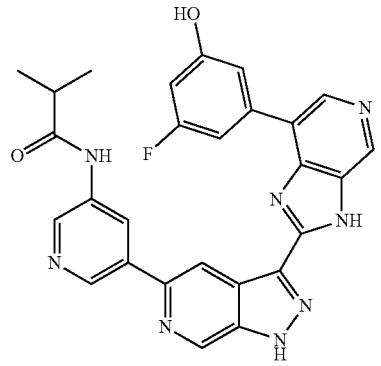
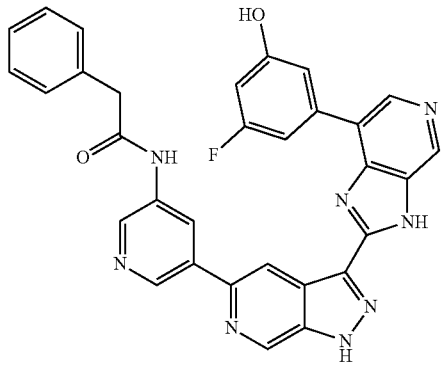
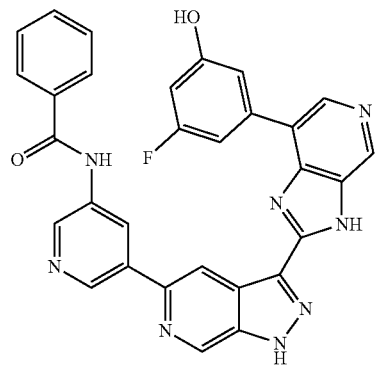
1286	
1287	
1288	
1289	

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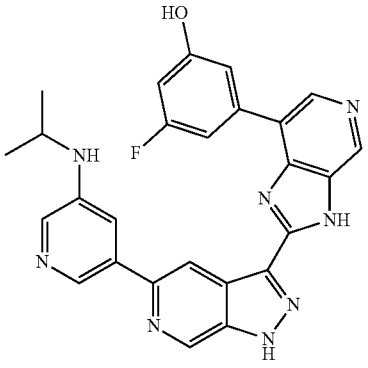
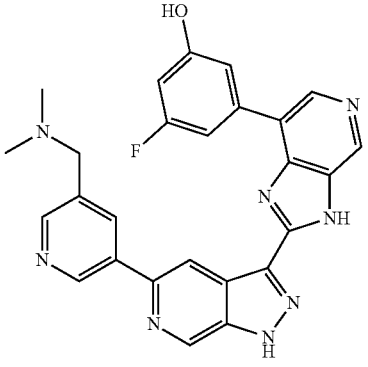
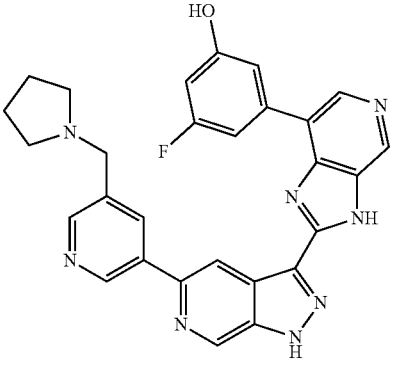
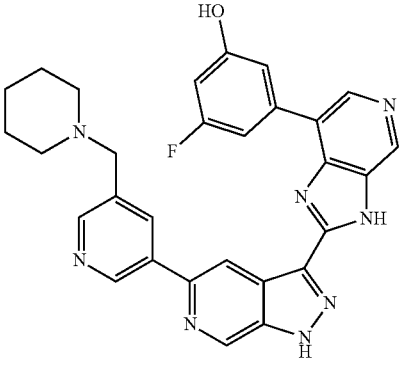
1290	
1291	
1292	
1293	

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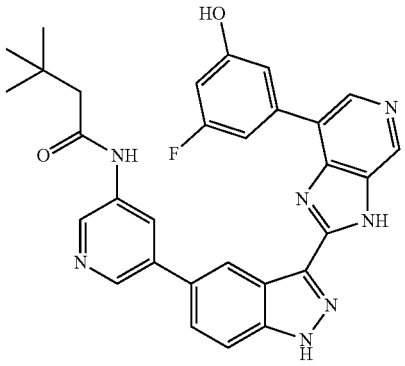
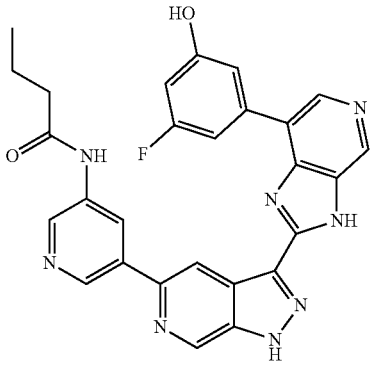
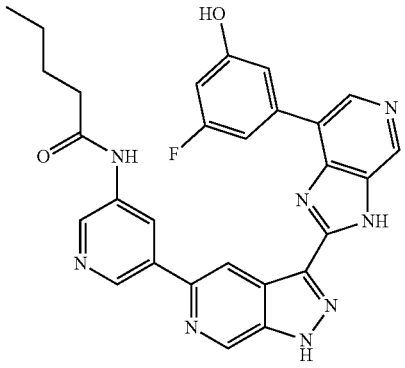
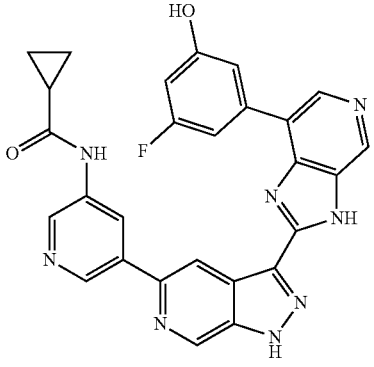
1294	
1295	
1296	
1297	

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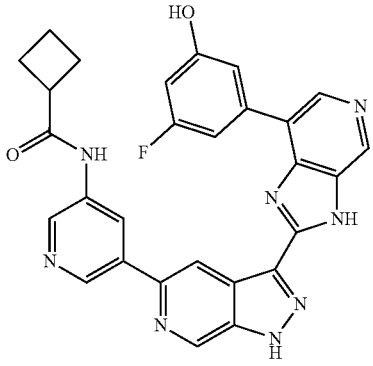
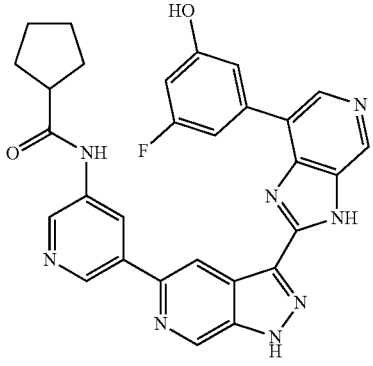
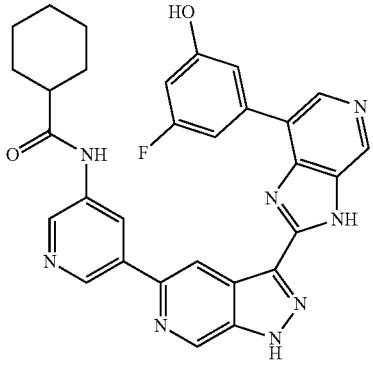
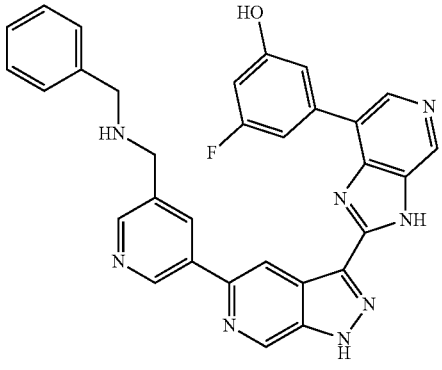
1298	
1299	
1300	
1301	

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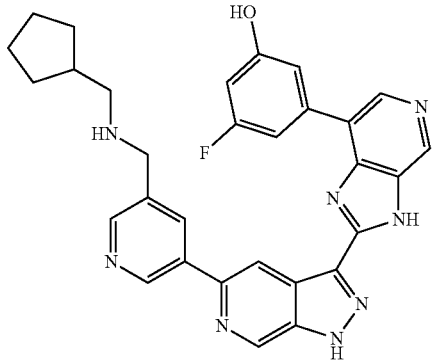
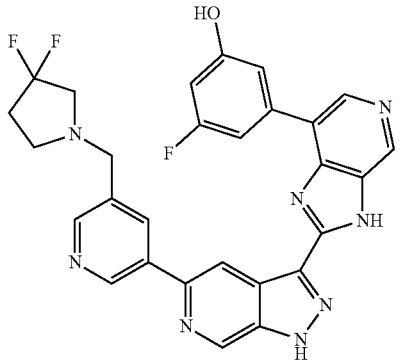
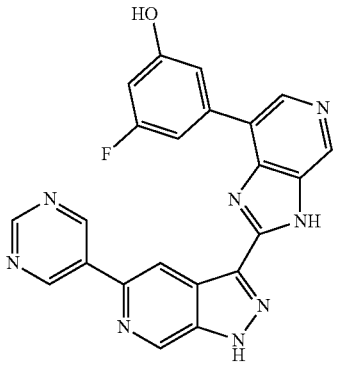
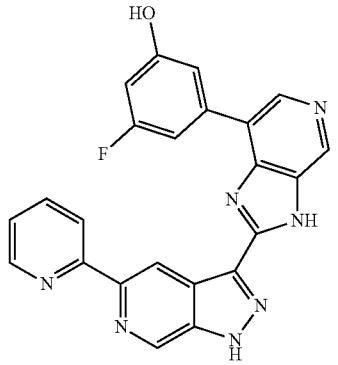
1302	
1303	
1304	
1305	

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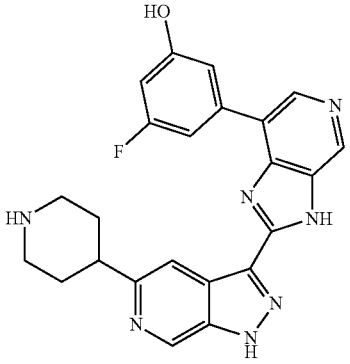
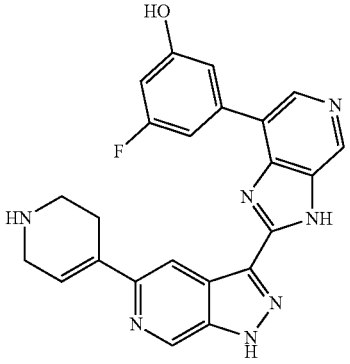
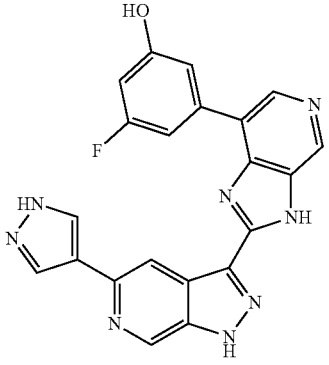
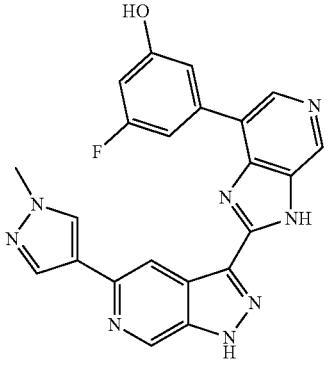
1306	
1307	
1308	
1309	

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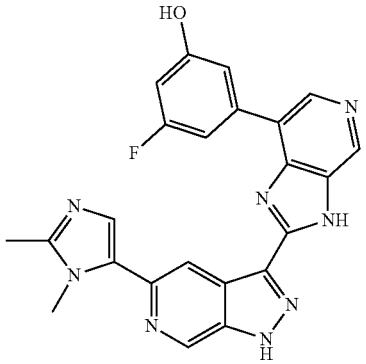
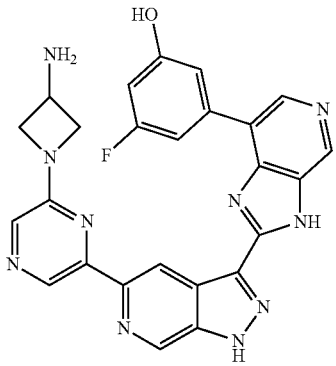
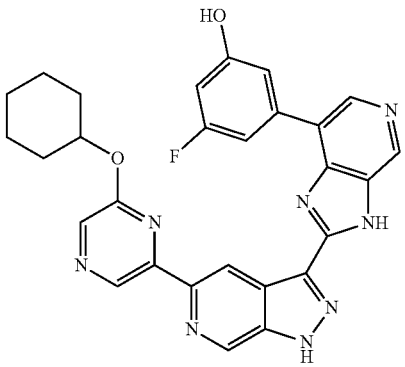
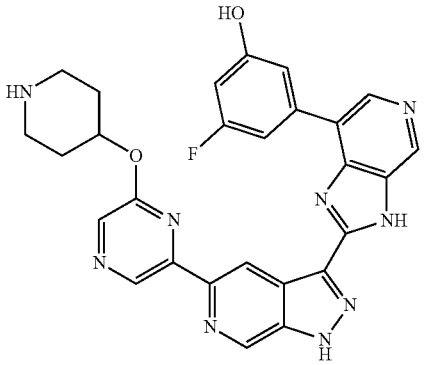
1310	
1311	
1312	
1313	

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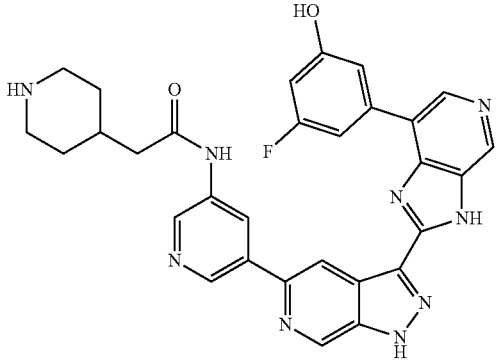
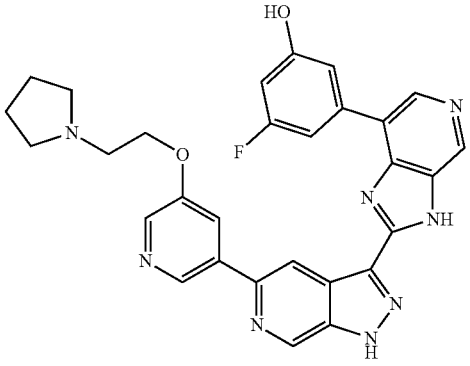
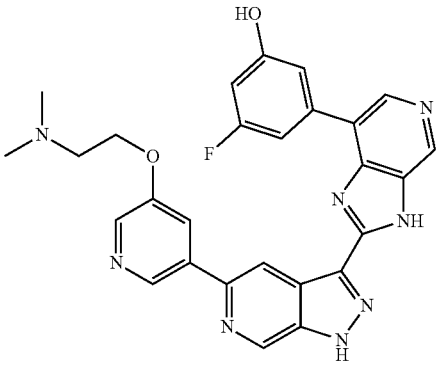
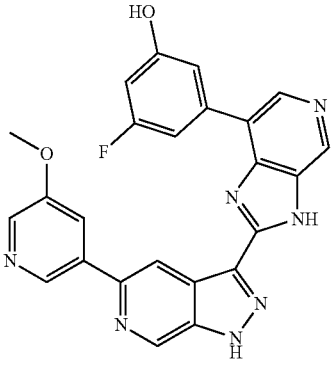
1314	
1315	
1316	
1317	

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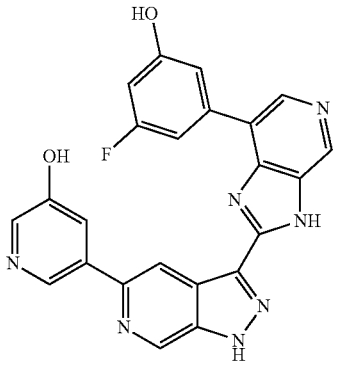
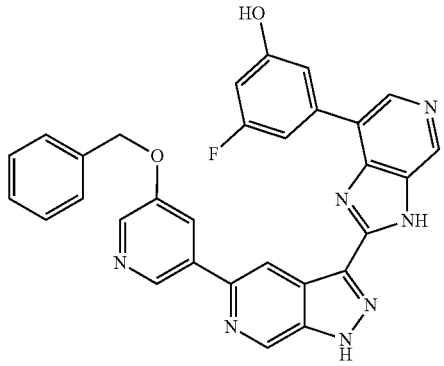
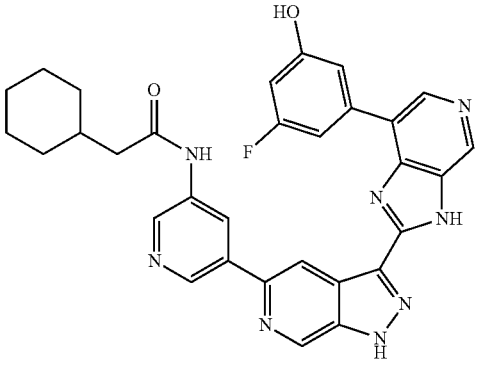
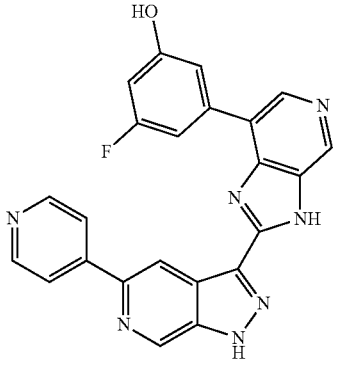
1318	
1319	
1320	
1321	

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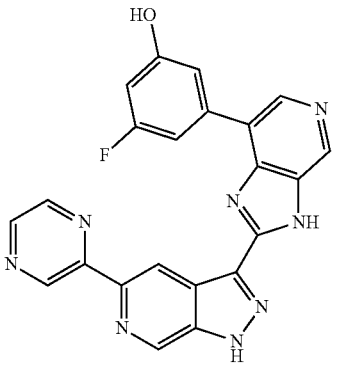
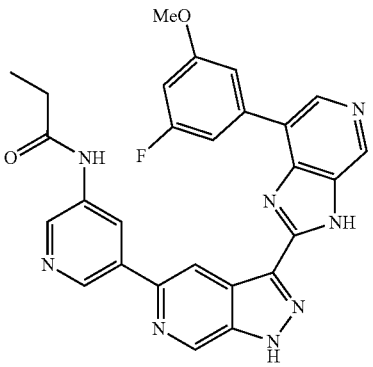
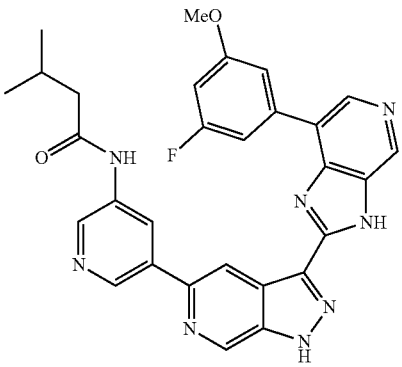
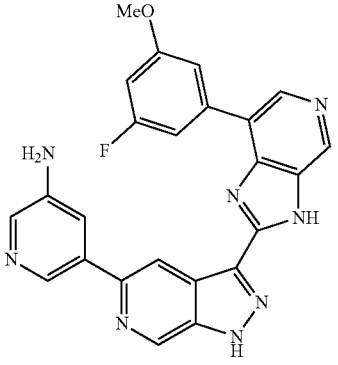
1322	
1323	
1324	
1325	

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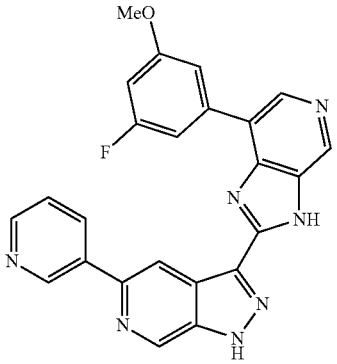
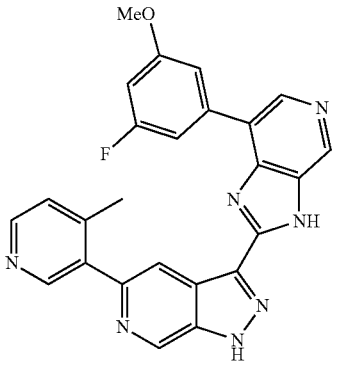
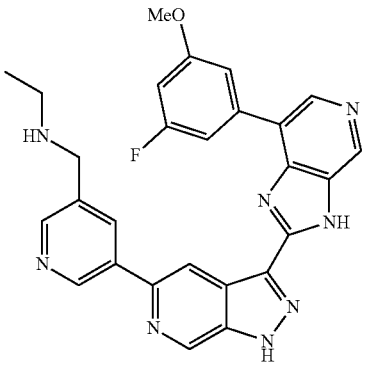
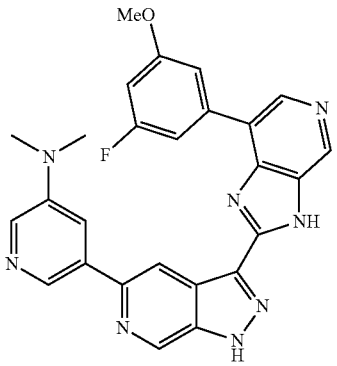
1326	
1327	
1328	
1329	

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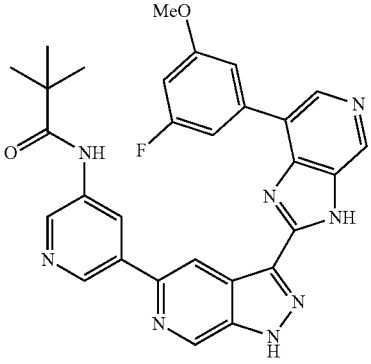
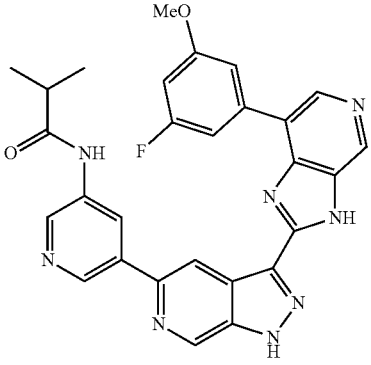
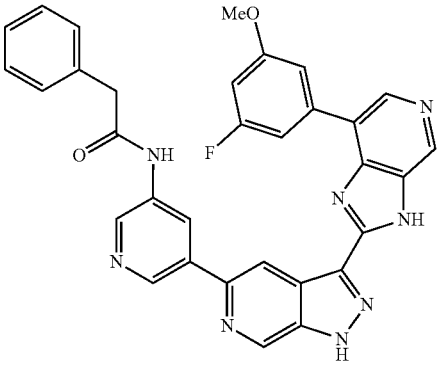
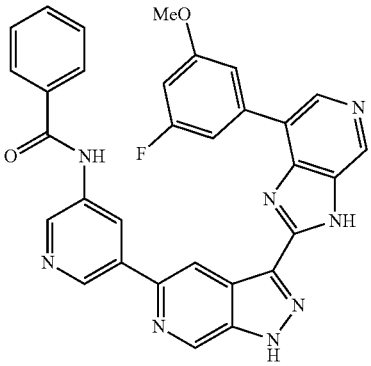
1330	
1331	
1332	
1333	

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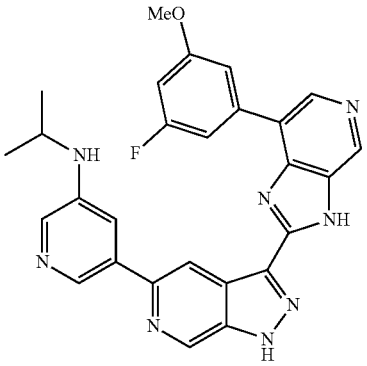
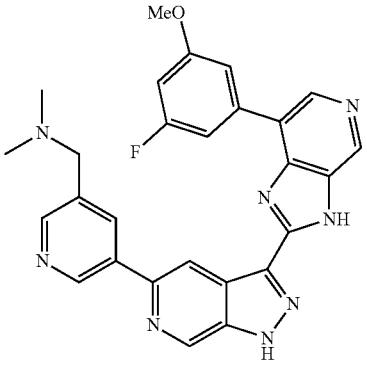
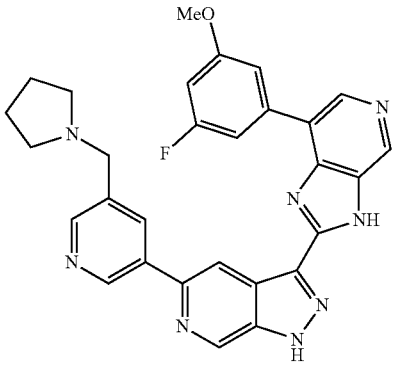
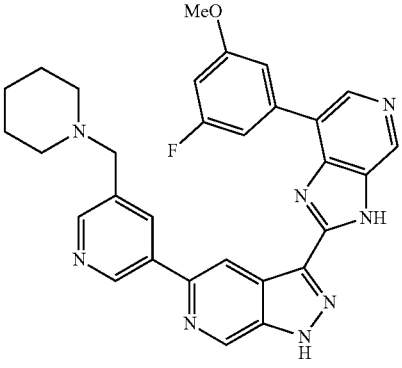
1334	
1335	
1336	
1337	

TABLE 1-continued

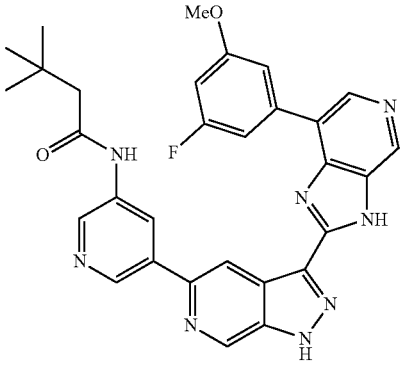
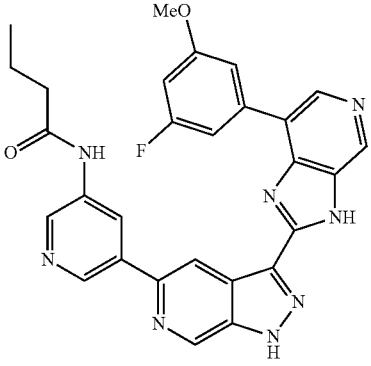
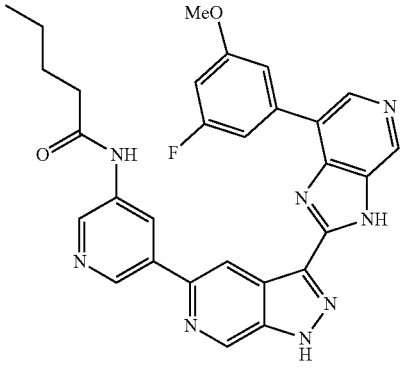
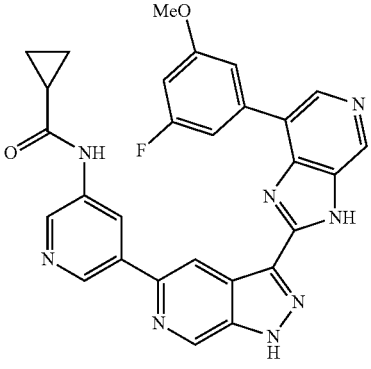
1338	
1339	
1340	
1341	

TABLE 1-continued

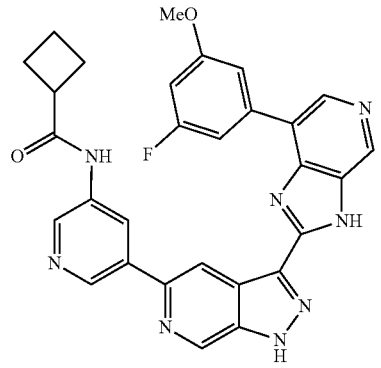
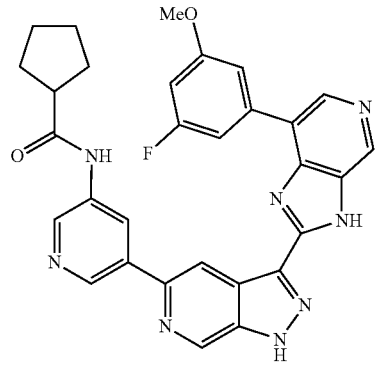
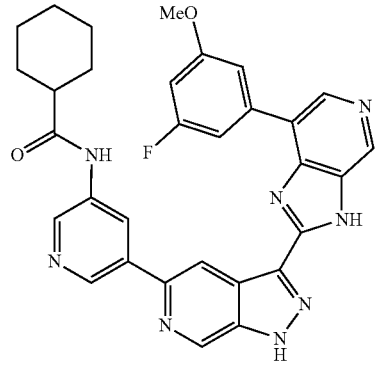
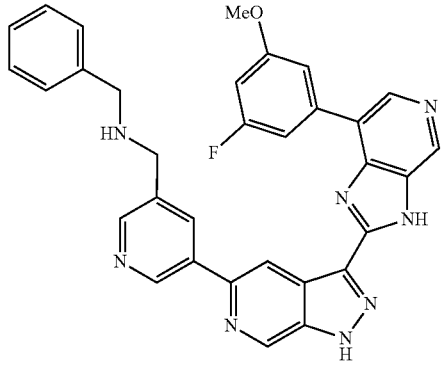
1342	
1343	
1344	
1345	

TABLE 1-continued

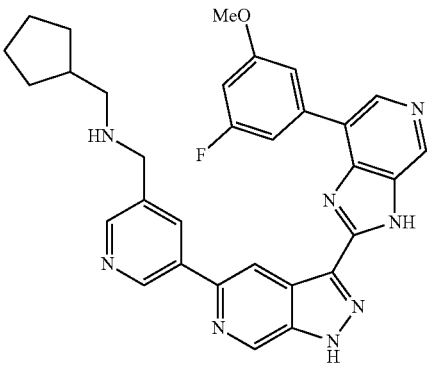
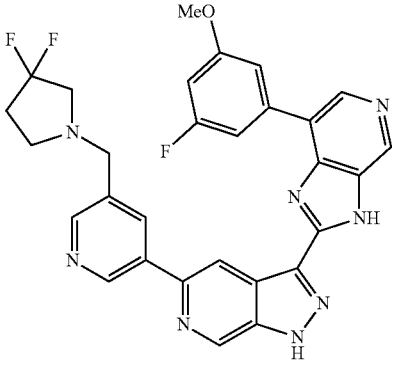
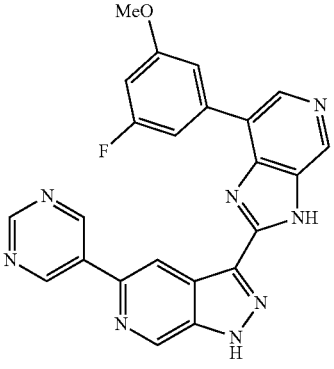
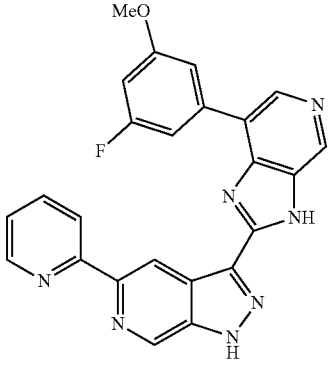
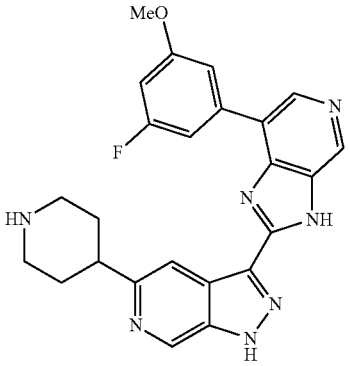
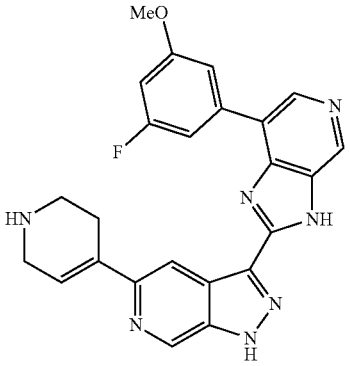
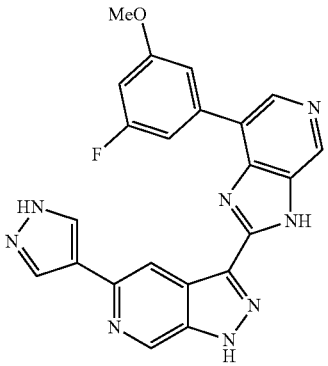
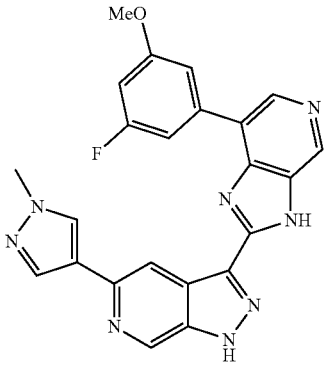
1346	
1347	
1348	
1349	

TABLE 1-continued

1350	
1351	
1352	
1353	

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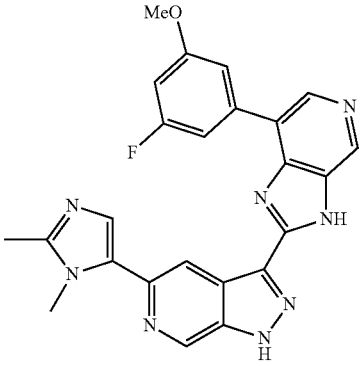
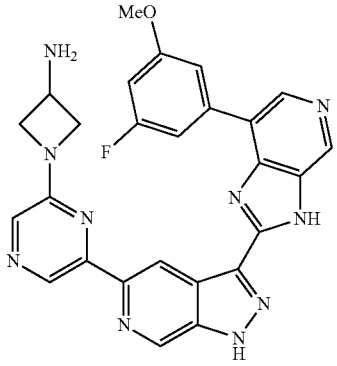
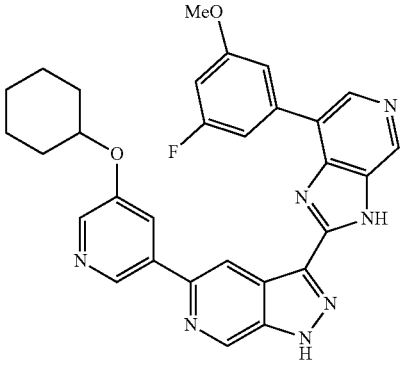
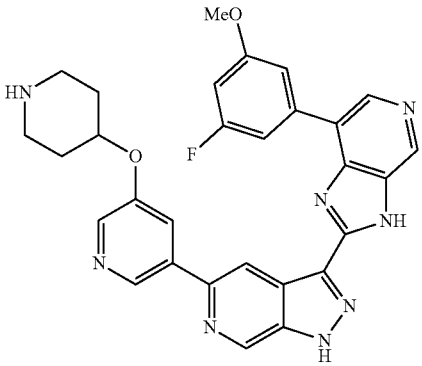
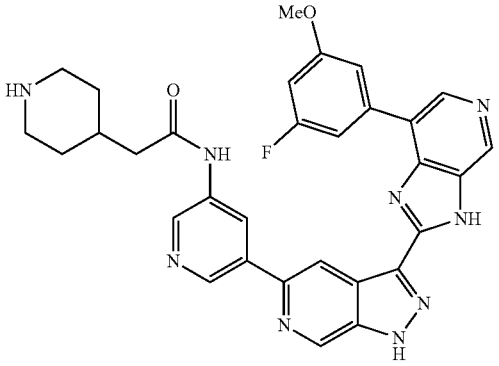
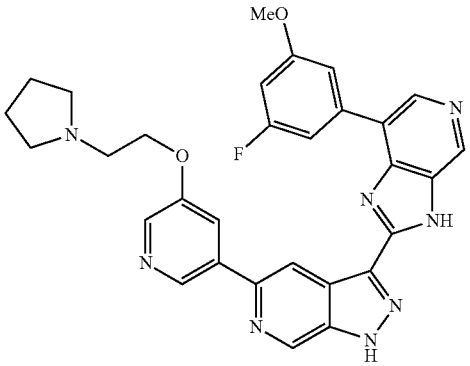
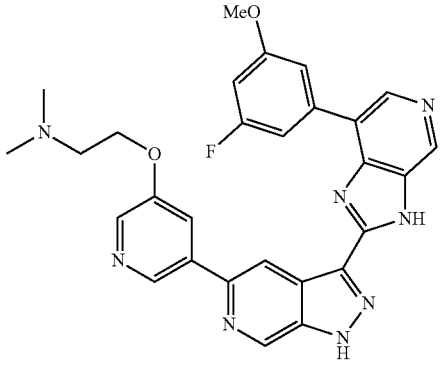
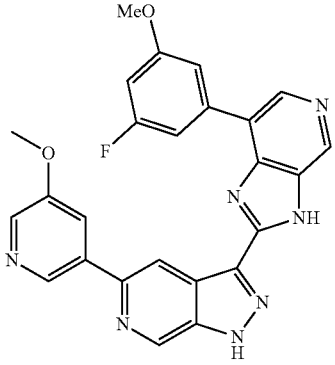
1354	
1355	
1356	
1357	

TABLE 1-continued

1358	
1359	
1360	
1361	

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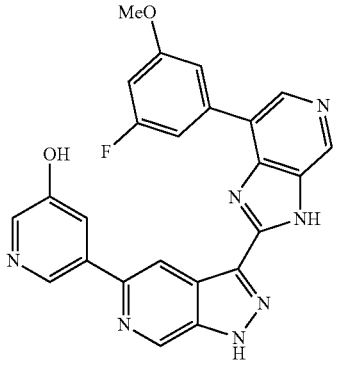
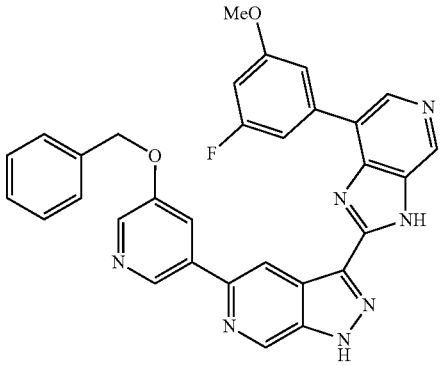
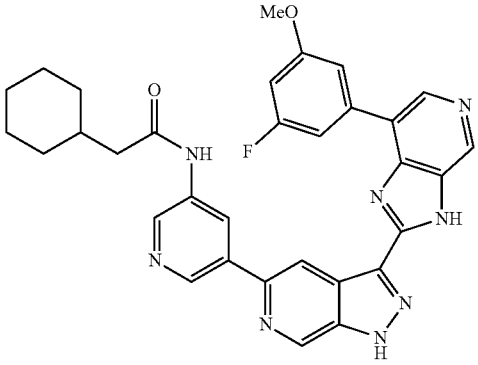
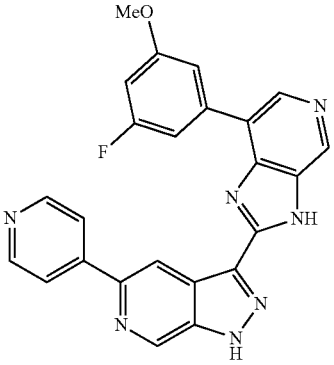
1362	
1363	
1364	
1365	

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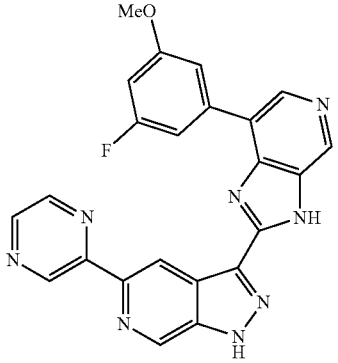
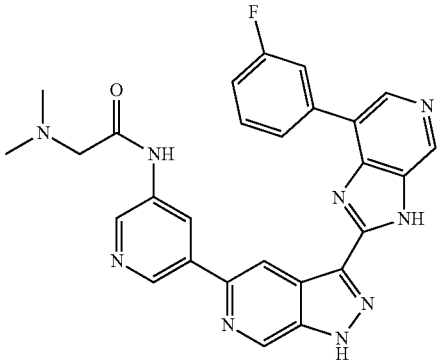
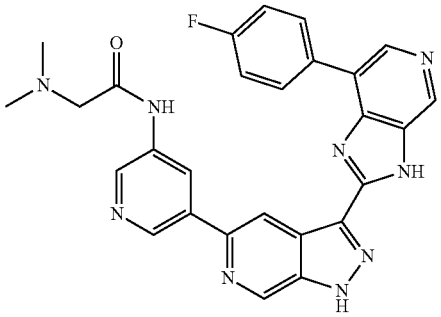
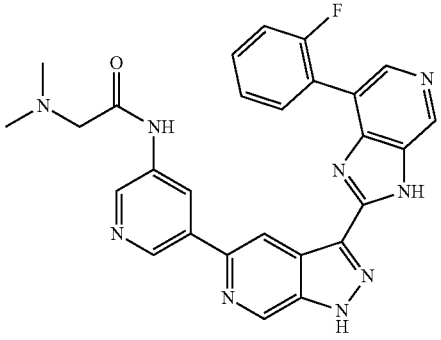
1366	
1367	
1368	
1369	

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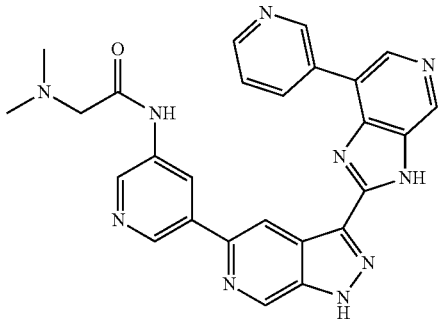
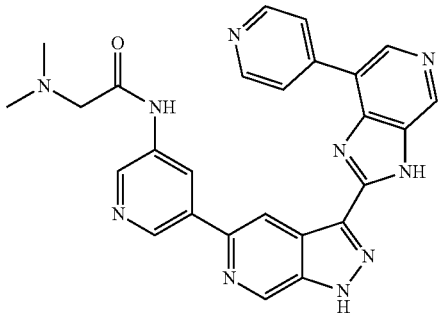
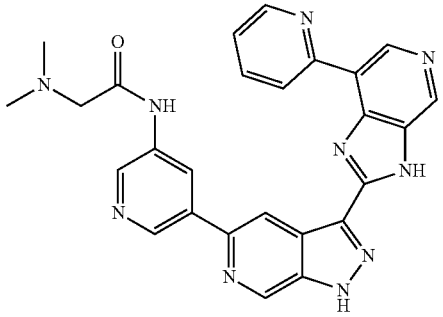
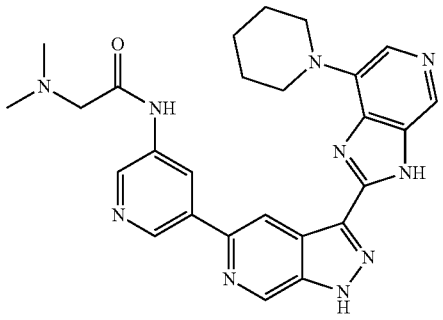
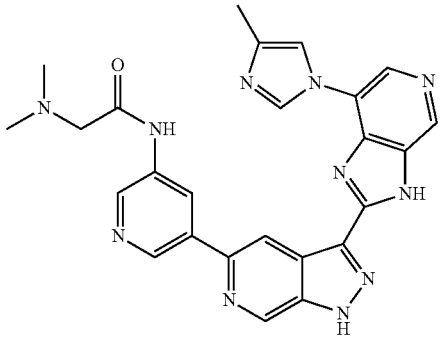
1370	
1371	
1372	
1373	
1374	

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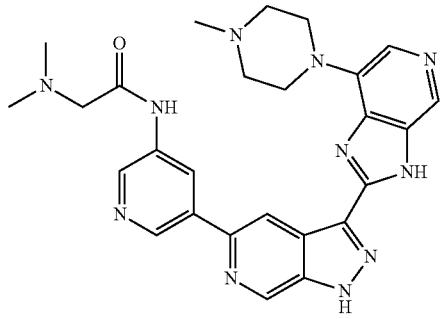
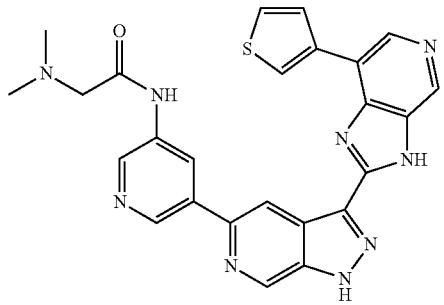
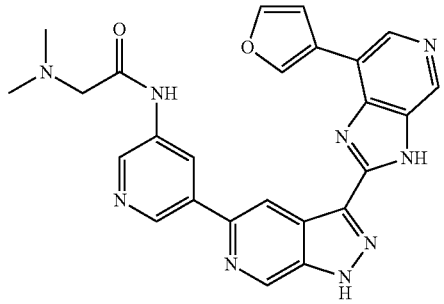
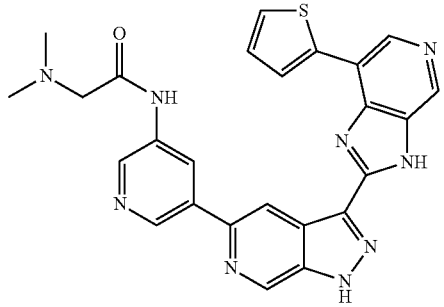
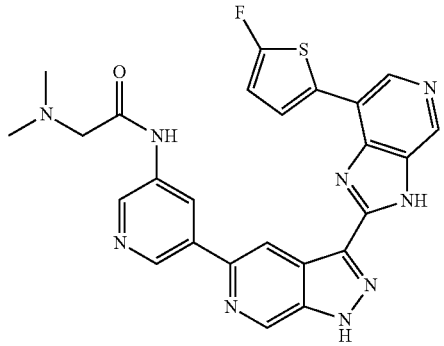
1375	
1376	
1377	
1378	
1379	

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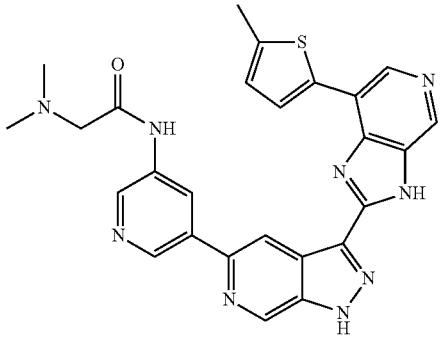
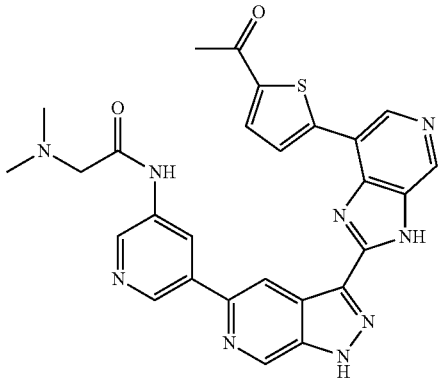
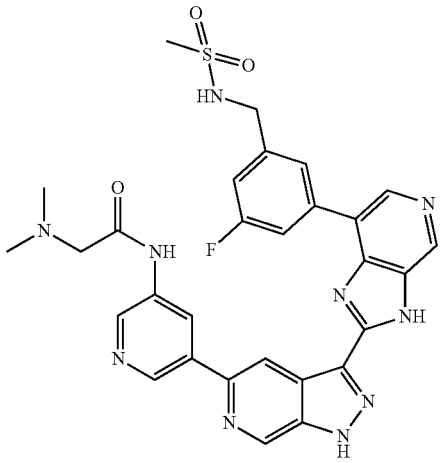
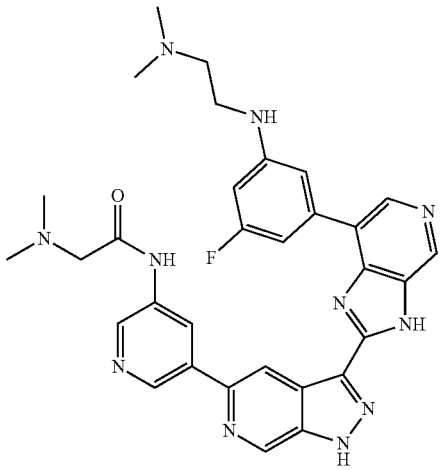
1380	
1381	
1382	
1383	

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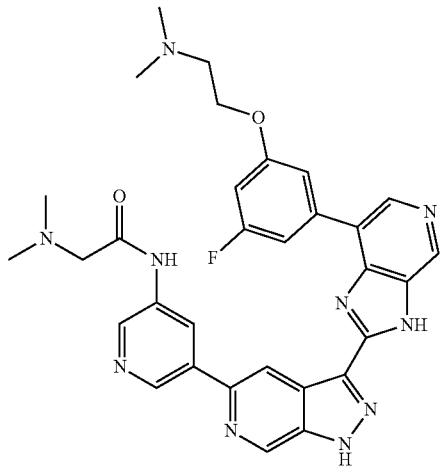
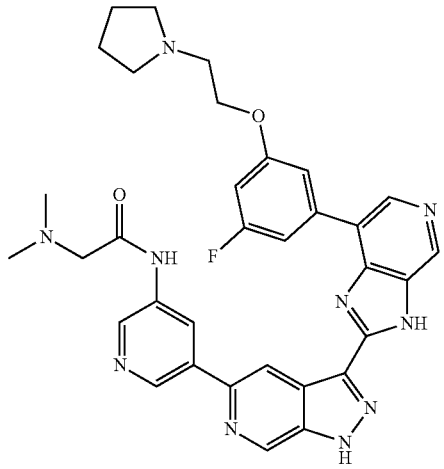
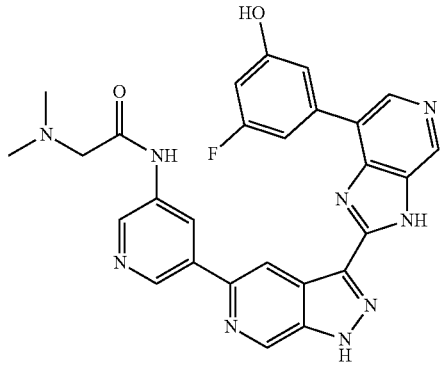
1384	
1385	
1386	

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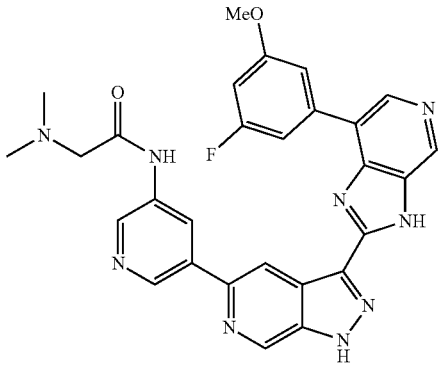
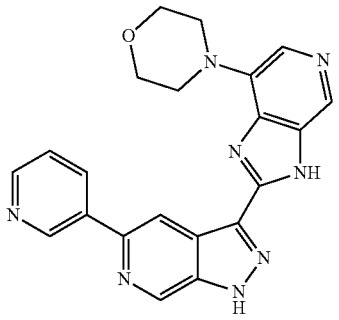
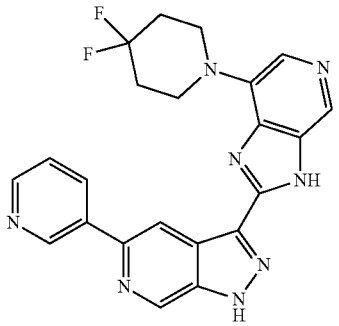
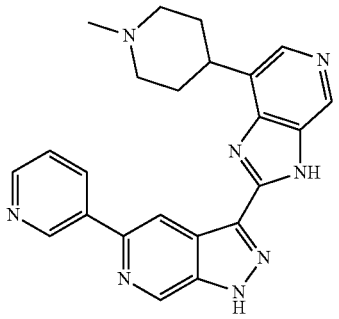
1387	
1388	
1389	
1390	

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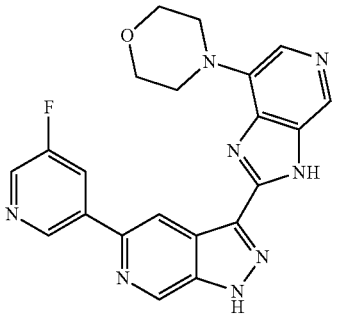
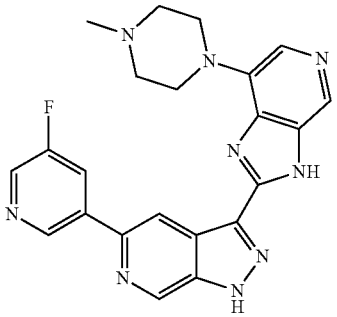
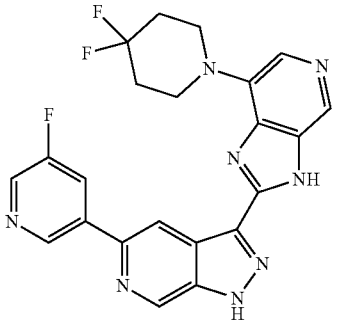
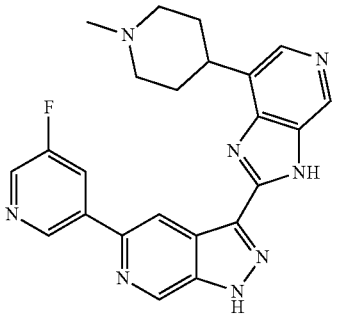
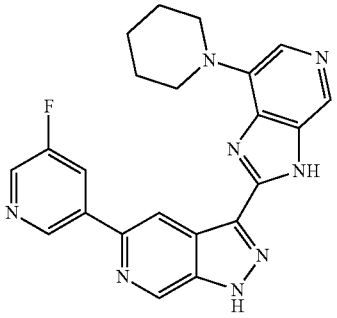
1391	
1392	
1393	
1394	
1395	

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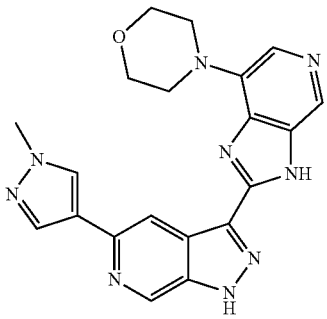
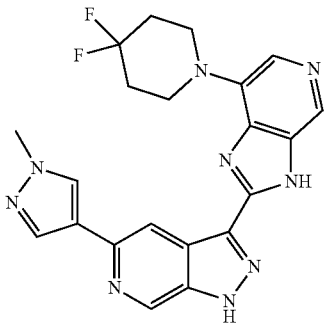
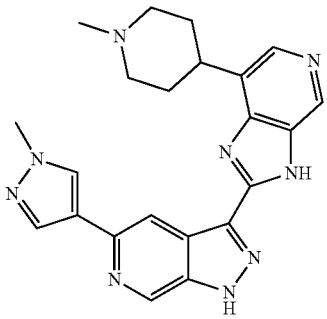
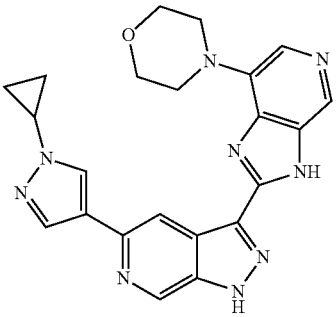
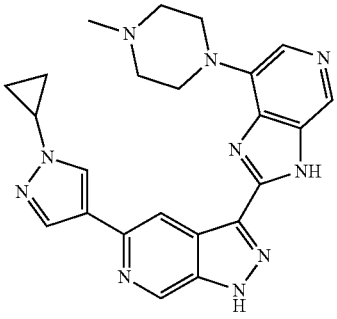
1396	
1397	
1398	
1399	
1400	

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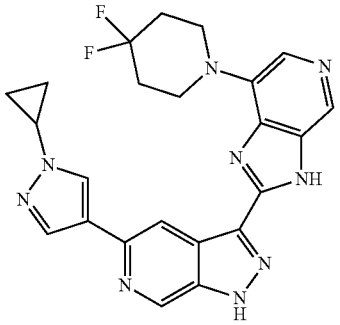
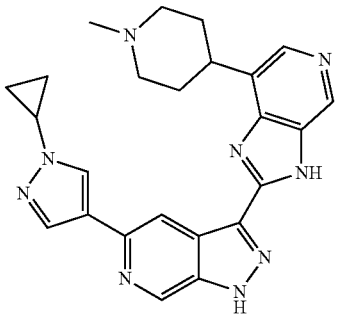
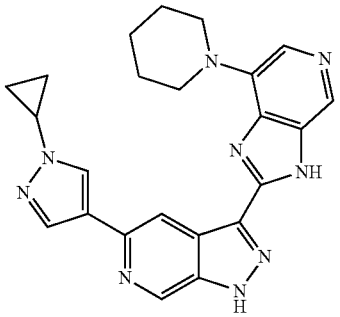
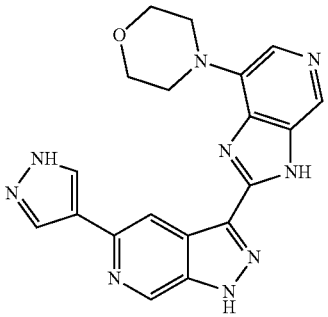
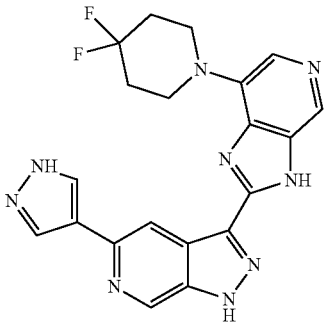
1401	
1402	
1403	
1404	
1405	

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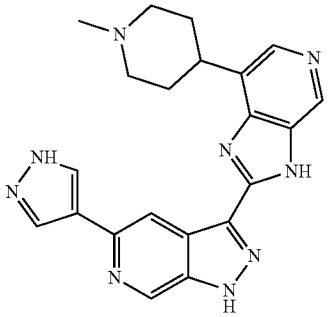
1406	

Administration and Pharmaceutical Compositions

Some embodiments include pharmaceutical compositions comprising: (a) a therapeutically effective amount of a compound provided herein, or its corresponding enantiomer, diastereoisomer or tautomer, or pharmaceutically acceptable salt; and (b) a pharmaceutically acceptable carrier.

The compounds provided herein may also be useful in combination (administered together or sequentially) with other known agents.

Non-limiting examples of diseases which can be treated with a combination of a compound of Formula (I) and other known agents are colorectal cancer, ovarian cancer, retinitis pigmentosa, macular degeneration, diabetic retinopathy, idiopathic pulmonary fibrosis/pulmonary fibrosis, and osteoarthritis.

In some embodiments, colorectal cancer can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: 5-Fluorouracil (5-FU), which can be administered with the vitamin-like drug leucovorin (also called folinic acid); capecitabine (XELODA®), irinotecan (CAMPOSTAR®), oxaliplatin (ELOXATIN®). Examples of combinations of these drugs which could be further combined with a compound of Formula (I) are FOLFOX (5-FU, leucovorin, and oxaliplatin), FOLFIRI (5-FU, leucovorin, and irinotecan), FOLFOXIRI (leucovorin, 5-FU, oxaliplatin, and irinotecan) and CapeOx (Capecitabine and oxaliplatin). For rectal cancer, chemo with 5-FU or capecitabine combined with radiation may be given before surgery (neoadjuvant treatment).

In some embodiments, ovarian cancer can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: Topotecan, Liposomal doxorubicin (DOXIL®), Gemcitabine (GEMZAR®), Cyclophosphamide (CYTOXAN®), Vinorelbine (NAVELBINE®), Ifosfamide (IFEX®), Etoposide (VP-16), Altretamine (HEXALEN®), Capecitabine (XELODA®), Irinotecan (CPT-11, CAMPTOSAR®), Melphalan, Pemetrexed (ALIMTA®) and Albumin bound paclitaxel (nab-paclitaxel, ABRAXANE®). Examples of combinations of these drugs which could be further combined with a compound of Formula (I) are TIP (paclitaxel [Taxol], ifosfamide, and cisplatin), VeIP (vinblastine, ifosfamide, and cisplatin) and VIP (etoposide [VP-16], ifosfamide, and cisplatin).

In some embodiments, a compound of Formula (I) can be used to treat cancer in combination with any of the following methods: (a) Hormone therapy such as aromatase inhibitors, LHRH [luteinizing hormone-releasing hormone] analogs and inhibitors, and others; (b) Ablation or embolization procedures such as radiofrequency ablation (RFA), ethanol (alcohol) ablation, microwave thermotherapy and cryosurgery (cryotherapy); (c) Chemotherapy using alkylating

agents such as cisplatin and carboplatin, oxaliplatin, mechlorethamine, cyclophosphamide, chlorambucil and ifosfamide; (d) Chemotherapy using anti-metabolites such as azathioprine and mercaptopurine; (e) Chemotherapy using plant alkaloids and terpenoids such as vinca alkaloids (i.e. Vincristine, Vinblastine, Vinorelbine and Vindesine) and taxanes; (f) Chemotherapy using podophyllotoxin, etoposide, teniposide and docetaxel; (g) Chemotherapy using topoisomerase inhibitors such as irinotecan, topotecan, amsacrine, etoposide, etoposide phosphate, and teniposide; (h) Chemotherapy using cytotoxic antibiotics such as actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin and mitomycin; (i) Chemotherapy using tyrosine-kinase inhibitors such as Imatinib mesylate (GLEEVEC®, also known as STI-571), Gefitinib (Iressa, also known as ZD1839), Erlotinib (marketed as TARCEVA®), Bortezomib (VELCADE®), tamoxifen, tofacitinib, crizotinib, Bcl-2 inhibitors (e.g. obatoclax in clinical trials, ABT-263, and Gossypol), PARP inhibitors (e.g. Iniparib, Olaparib in clinical trials), PI3K inhibitors (eg. perifosine in a phase III trial), VEGF Receptor 2 inhibitors (e.g. Apatinib), AN-152, (AEZS-108), Braf inhibitors (e.g. vemurafenib, dabrafenib and LGX818), MEK inhibitors (e.g. trametinib and MEK162), CDK inhibitors, (e.g. PD-0332991), salinomycin and Sorafenib; (j) Chemotherapy using monoclonal antibodies such as Rituximab (marketed as MABTHERA® or RITUXAN®), Trastuzumab (Herceptin also known as ErbB2), Cetuximab (marketed as ERBITUX®), and Bevacizumab (marketed as AVASTIN®); and (k) radiation therapy.

In some embodiments, diabetic retinopathy can be treated with a combination of a compound of Formula (I) and one or more of the following natural supplements: Bilberry, Butcher's broom, Ginkgo, Grape seed extract, and Pycnogenol (Pine bark).

In some embodiments, idiopathic pulmonary fibrosis/pulmonary fibrosis can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: pirfenidone (pirfenidone was approved for use in 2011 in Europe under the brand name Esbriet®), prednisone, azathioprine, N-acetylcysteine, interferon-γ 1b, bosentan (bosentan is currently being studied in patients with IPF, [*The American Journal of Respiratory and Critical Care Medicine* (2011), 184(1), 92-9]), Nintedanib (BIBF 1120 and Vargatef), QAX576 *[British Journal of Pharmacology* (2011), 163(1), 141-172], and anti-inflammatory agents such as corticosteroids.

In some embodiments, a compound of Formula (I) can be used to treat idiopathic pulmonary fibrosis/pulmonary fibrosis in combination with any of the following methods: oxygen therapy, pulmonary rehabilitation and surgery.

In some embodiments, a compound of Formula (I) can be used to treat osteoarthritis in combination with any of the following methods: (a) Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen, aspirin and acetaminophen; (b) physical therapy; (c) injections of corticosteroid medications; (d) injections of hyaluronic acid derivatives (e.g. Hyalgan, Synvisc); (e) narcotics, like codeine; (f) in combination with braces and/or shoe inserts or any device that can immobilize or support your joint to help you keep pressure off it (e.g., splints, braces, shoe inserts or other medical devices); (g) realigning bones (osteotomy); (h) joint replacement (arthroplasty); and (i) in combination with a chronic pain class.

In some embodiments, macular degeneration can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: Bevacizumab (Avastin®), Ranibizumab (Lucentis®), Pegaptanib (Macugen), Aflibercept (Eylea®), verteporfin (Visudyne®) in combination with photodynamic therapy (PDT) or with any of the following methods: (a) in combination with laser to destroy abnormal blood vessels (photocoagulation); and (b) in combination with increased vitamin intake of antioxidant vitamins and zinc.

In some embodiments, retinitis pigmentosa can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: UF-021 (Ocuseva™), vitamin A palmitate and pikachurin or with any of the following methods: (a) with the Argus® II retinal implant; and (b) with stem cell and/or gene therapy.

Administration of the compounds disclosed herein or the pharmaceutically acceptable salts thereof can be via any of the accepted modes of administration, including, but not limited to, orally, subcutaneously, intravenously, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonarilly, vaginally, rectally, ontologically, neuro-otologically, intraocularly, subconjuctivally, via anterior eye chamber injection, intravitreally, intraperitoneally, intrathecally, intracystically, intrapleurally, via wound irrigation, intrabuccally, intra-abdominally, intra-articularly, intra-aurally, intrabronchially, intracapsularly, intrameningeally, via inhalation, via endotracheal or endobronchial instillation, via direct instillation into pulmonary cavities, intraspinally, intrasynovially, intrathoracically, via thoracostomy irrigation, epidurally, intratympanically, intracisternally, intravascularly, intraventricularly, intraosseously, via irrigation of infected bone, or via application as part of any admixture with a prosthetic devices. In some embodiments, the administration method includes oral or parenteral administration.

Compounds provided herein intended for pharmaceutical use may be administered as crystalline or amorphous products. Pharmaceutically acceptable compositions may include solid, semi-solid, liquid, solutions, colloidal, liposomes, emulsions, suspensions, complexes, coacervates and aerosols. Dosage forms, such as, e.g., tablets, capsules, powders, liquids, suspensions, suppositories, aerosols, implants, controlled release or the like. They may be obtained, for example, as solid plugs, powders, or films by methods such as precipitation, crystallization, milling, grinding, supercritical fluid processing, coacervation, complex coacervation, encapsulation, emulsification, complexation, freeze drying, spray drying, or evaporative drying. Microwave or radio frequency drying may be used for this purpose. The compounds can also be administered in sustained or controlled release dosage forms, including depot injections, osmotic pumps, pills (tablets and or capsules), transdermal (including electrotransport) patches, implants and the like, for prolonged and/or timed, pulsed administration at a predetermined rate.

The compounds can be administered either alone or in combination with a conventional pharmaceutical carrier, excipient or the like. Pharmaceutically acceptable excipients include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, self-emulsifying drug delivery systems (SEDDS) such as d-α-tocopherol polyethylene glycol 1000 succinate, surfactants used in pharmaceutical dosage forms such as Tweens, poloxamers or other similar polymeric delivery matrices, serum proteins, such as human serum albumin, buffer substances such as phosphates, tris, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium-chlo-

ride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethyl cellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, and wool fat. Cyclodextrins such as α-, β, and γ-cyclodextrin, or chemically modified derivatives such as hydroxyalkylcyclodextrins, including 2- and 3-hydroxypropyl-β-cyclodextrins, or other solubilized derivatives can also be used to enhance delivery of compounds described herein. Dosage forms or compositions containing a compound as described herein in the range of 0.005% to 100% with the balance made up from non-toxic carrier may be prepared. The contemplated compositions may contain 0.001%-100% of a compound provided herein, in one embodiment 0.1-95%, in another embodiment 75-85%, in a further embodiment 20-80%. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see *Remington: The Science and Practice of Pharmacy,* 22nd Edition (Pharmaceutical Press, London, U K. 2012).

In one embodiment, the compositions will take the form of a unit dosage form such as a pill or tablet and thus the composition may contain, along with a compound provided herein, a diluent such as lactose, sucrose, dicalcium phosphate, or the like; a lubricant such as magnesium stearate or the like; and a binder such as starch, gum acacia, polyvinylpyrrolidine, gelatin, cellulose, cellulose derivatives or the like. In another solid dosage form, a powder, marume, solution or suspension (e.g., in propylene carbonate, vegetable oils, PEG's, poloxamer 124 or triglycerides) is encapsulated in a capsule (gelatin or cellulose base capsule). Unit dosage forms in which one or more compounds provided herein or additional active agents are physically separated are also contemplated; e.g., capsules with granules (or tablets in a capsule) of each drug; two-layer tablets; two-compartment gel caps, etc. Enteric coated or delayed release oral dosage forms are also contemplated.

Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, etc. a compound provided herein and optional pharmaceutical adjuvants in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) to form a solution, colloid, liposome, emulsion, complexes, coacervate or suspension. If desired, the pharmaceutical composition can also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, co-solvents, solubilizing agents, pH buffering agents and the like (e.g., sodium acetate, sodium citrate, cyclodextrin derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine oleate, and the like).

In some embodiments, the unit dosage of compounds of Formula (I) is about 0.25 mg/Kg to about 50 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 0.25 mg/Kg to about 20 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 0.50 mg/Kg to about 19 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 0.75 mg/Kg to about 18 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 1.0 mg/Kg to about 17 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 1.25 mg/Kg to about 16 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 1.50 mg/Kg to about 15 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 1.75 mg/Kg to about 14 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 2.0 mg/Kg to about 13 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 3.0 mg/Kg to about 12 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 4.0 mg/Kg to about 11 mg/Kg in humans.

In some embodiments, the unit dosage of compounds of Formula (I) is about 5.0 mg/Kg to about 10 mg/Kg in humans.

In some embodiments, the compositions are provided in unit dosage forms suitable for single administration.

In some embodiments, the compositions are provided in unit dosage forms suitable for twice a day administration.

In some embodiments, the compositions are provided in unit dosage forms suitable for three times a day administration.

Injectables can be prepared in conventional forms, either as liquid solutions, colloid, liposomes, complexes, coacervate or suspensions, as emulsions, or in solid forms suitable for reconstitution in liquid prior to injection. The percentage of a compound provided herein contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the compound and the needs of the patient. However, percentages of active ingredient of 0.01% to 10% in solution are employable, and could be higher if the composition is a solid or suspension, which could be subsequently diluted to the above percentages.

In some embodiments, the composition will comprise about 0.1-10% of the active agent in solution.

In some embodiments, the composition will comprise about 0.1-5% of the active agent in solution.

In some embodiments, the composition will comprise about 0.1-4% of the active agent in solution.

In some embodiments, the composition will comprise about 0.15-3% of the active agent in solution.

In some embodiments, the composition will comprise about 0.2-2% of the active agent in solution.

In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-96 hours.

In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-72 hours.

In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-48 hours.

In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-24 hours.

In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-12 hours.

In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-6 hours.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 5 mg/m^2 to about 300 mg/m^2.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 5 mg/m^2 to about 200 mg/m^2.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 5 mg/m^2 to about 100 mg/m^2.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 10 mg/m^2 to about 50 mg/m^2.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 50 mg/m^2 to about 200 mg/m^2.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 75 mg/m^2 to about 175 mg/m^2.

In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 100 mg/m^2 to about 150 mg/m^2.

It is to be noted that concentrations and dosage values may also vary depending on the specific compound and the severity of the condition to be alleviated. It is to be further understood that for any particular patient, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

In one embodiment, the compositions can be administered to the respiratory tract (including nasal and pulmonary) e.g., through a nebulizer, metered-dose inhalers, atomizer, mister, aerosol, dry powder inhaler, insufflator, liquid instillation or other suitable device or technique.

In some embodiments, aerosols intended for delivery to the nasal mucosa are provided for inhalation through the nose. For optimal delivery to the nasal cavities, inhaled particle sizes of about 5 to about 100 microns are useful, with particle sizes of about 10 to about 60 microns being preferred. For nasal delivery, a larger inhaled particle size may be desired to maximize impaction on the nasal mucosa and to minimize or prevent pulmonary deposition of the administered formulation. In some embodiments, aerosols intended for delivery to the lung are provided for inhalation through the nose or the mouth. For delivery to the lung, inhaled aerodynamic particle sizes of about less than 10 μm are useful (e.g., about 1 to about 10 microns). Inhaled particles may be defined as liquid droplets containing dissolved drug, liquid droplets containing suspended drug particles (in cases where the drug is insoluble in the suspending medium), dry particles of pure drug substance, drug substance incorporated with excipients, liposomes, emulsions, colloidal systems, coacervates, aggregates of drug nanoparticles, or dry particles of a diluent which contain embedded drug nanoparticles.

In some embodiments, compounds of Formula (I) disclosed herein intended for respiratory delivery (either systemic or local) can be administered as aqueous formulations, as non-aqueous solutions or suspensions, as suspensions or solutions in halogenated hydrocarbon propellants with or without alcohol, as a colloidal system, as emulsions, coacervates, or as dry powders. Aqueous formulations may be aerosolized by liquid nebulizers employing either hydraulic or ultrasonic atomization or by modified micropump systems (like the soft mist inhalers, the Aerodose® or the AERx® systems). Propellant-based systems may use suitable pressurized metered-dose inhalers (pMDIs). Dry powders may use dry powder inhaler devices (DPIs), which are capable of dispersing the drug substance effectively. A desired particle size and distribution may be obtained by choosing an appropriate device.

In some embodiments, the compositions of Formula (I) disclosed herein can be administered to the ear by various methods. For example, a round window catheter (e.g., U.S. Pat. Nos. 6,440,102 and 6,648,873) can be used.

Alternatively, formulations can be incorporated into a wick for use between the outer and middle ear (e.g., U.S. Pat. No. 6,120,484) or absorbed to collagen sponge or other solid support (e.g., U.S. Pat. No. 4,164,559).

If desired, formulations of the invention can be incorporated into a gel formulation (e.g., U.S. Pat. Nos. 4,474,752 and 6,911,211).

In some embodiments, compounds of Formula (I) disclosed herein intended for delivery to the ear can be administered via an implanted pump and delivery system through a needle directly into the middle or inner ear (cochlea) or through a cochlear implant stylet electrode channel or alternative prepared drug delivery channel such as but not limited to a needle through temporal bone into the cochlea.

Other options include delivery via a pump through a thin film coated onto a multichannel electrode or electrode with a specially imbedded drug delivery channel (pathways) carved into the thin film for this purpose. In other embodiments the acidic or basic solid compound of Formula (I) can be delivered from the reservoir of an external or internal implanted pumping system.

Formulations of the invention also can be administered to the ear by intratympanic injection into the middle ear, inner ear, or cochlea (e.g., U.S. Pat. No. 6,377,849 and Ser. No. 11/337,815).

Intratympanic injection of therapeutic agents is the technique of injecting a therapeutic agent behind the tympanic membrane into the middle and/or inner ear. In one embodiment, the formulations described herein are administered directly onto the round window membrane via transtympanic injection. In another embodiment, the ion channel modulating agent auris-acceptable formulations described herein are administered onto the round window membrane via a non-transtympanic approach to the inner ear. In additional embodiments, the formulation described herein is administered onto the round window membrane via a surgical approach to the round window membrane comprising modification of the crista fenestrae cochleae.

In some embodiments, the compounds of Formula (I) are formulated in rectal compositions such as enemas, rectal gels, rectal foams, rectal aerosols, suppositories, jelly suppositories, or retention enemas, containing conventional suppository bases such as cocoa butter or other glycerides, as well as synthetic polymers such as polyvinylpyrrolidone, PEG (like PEG ointments), and the like.

Suppositories for rectal administration of the drug (either as a solution, colloid, suspension or a complex) can be prepared by mixing a compound provided herein with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt or erode/dissolve in the rectum and release the compound. Such materials include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, poloxamers, mixtures of polyethylene glycols of various molecular weights and fatty acid esters of polyethylene glycol. In suppository forms of the compositions, a low-melting wax

such as, but not limited to, a mixture of fatty acid glycerides, optionally in combination with cocoa butter, is first melted.

Solid compositions can be provided in various different types of dosage forms, depending on the physicochemical properties of the compound provided herein, the desired dissolution rate, cost considerations, and other criteria. In one of the embodiments, the solid composition is a single unit. This implies that one unit dose of the compound is comprised in a single, physically shaped solid form or article. In other words, the solid composition is coherent, which is in contrast to a multiple unit dosage form, in which the units are incoherent.

Examples of single units which may be used as dosage forms for the solid composition include tablets, such as compressed tablets, film-like units, foil-like units, wafers, lyophilized matrix units, and the like. In one embodiment, the solid composition is a highly porous lyophilized form. Such lyophilizates, sometimes also called wafers or lyophilized tablets, are particularly useful for their rapid disintegration, which also enables the rapid dissolution of the compound.

On the other hand, for some applications the solid composition may also be formed as a multiple unit dosage form as defined above. Examples of multiple units are powders, granules, microparticles, pellets, mini-tablets, beads, lyophilized powders, and the like. In one embodiment, the solid composition is a lyophilized powder. Such a dispersed lyophilized system comprises a multitude of powder particles, and due to the lyophilization process used in the formation of the powder, each particle has an irregular, porous microstructure through which the powder is capable of absorbing water very rapidly, resulting in quick dissolution. Effervescent compositions are also contemplated to aid the quick dispersion and absorption of the compound.

Another type of multiparticulate system which is also capable of achieving rapid drug dissolution is that of powders, granules, or pellets from water-soluble excipients which are coated with a compound provided herein so that the compound is located at the outer surface of the individual particles. In this type of system, the water-soluble low molecular weight excipient may be useful for preparing the cores of such coated particles, which can be subsequently coated with a coating composition comprising the compound and, for example, one or more additional excipients, such as a binder, a pore former, a saccharide, a sugar alcohol, a film-forming polymer, a plasticizer, or other excipients used in pharmaceutical coating compositions.

Also provided herein are kits. Typically, a kit includes one or more compounds or compositions as described herein. In certain embodiments, a kit can include one or more delivery systems, e.g., for delivering or administering a compound as provided herein, and directions for use of the kit (e.g., instructions for treating a patient). In another embodiment, the kit can include a compound or composition as described herein and a label that indicates that the contents are to be administered to a patient with cancer. In another embodiment, the kit can include a compound or composition as described herein and a label that indicates that the contents are to be administered to a patient with one or more of hepatocellular carcinoma, colon cancer, leukemia, lymphoma, sarcoma, ovarian cancer, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects and/or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

Methods of Treatment

The compounds and compositions provided herein can be used as inhibitors and/or modulators of one or more components of the Wnt pathway, which may include one or more Wnt proteins, and thus can be used to treat a variety of disorders and diseases in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, and cell cycling. Accordingly, the compounds and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation, to correct a genetic disorder, and/or to treat a neurological condition/disorder/disease due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, scleroderma, mycotic and viral infections, bone and cartilage diseases, neurological conditions/diseases such as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), motor neuron disease, multiple sclerosis or autism, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects and/or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

In some embodiments, non-limiting examples of eye diseases which can be treated with the compounds and compositions provided herein include age-related macular degeneration (AMD or ARMD), rod cone dystrophy, retinitis pigmentosa (RP), acute idiopathic blind spot enlargement (AIBSE), acute zonal occult outer retinopathy (AZOOR), acute macular neuroretinopathy (AMN), multiple evanescent white dot syndrome (MEWDS), multifocal choroiditis, opticneuropathy. Further causes of photoreceptor damage that can be treated with the compounds and compositions provided herein include retinal detachment, vascular disturbance, eye tumors or extreme light damage.

With respect to cancer, the Wnt pathway is known to be constitutively activated in a variety of cancers including, for

example, colon cancer, hepatocellular carcinoma, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer and leukemias such as CML, CLL and T-ALL. Accordingly, the compounds and compositions described herein may be used to treat these cancers in which the Wnt pathway is constitutively activated. In certain embodiments, the cancer is chosen from hepatocellular carcinoma, colon cancer, leukemia, lymphoma, sarcoma and ovarian cancer.

Other cancers can also be treated with the compounds and compositions described herein.

More particularly, cancers that may be treated by the compounds, compositions and methods described herein include, but are not limited to, the following:

1) Breast cancers, including, for example ER^+ breast cancer, ER^- breast cancer, $her2^-$ breast cancer, $her2^+$ breast cancer, stromal tumors such as fibroadenomas, phyllodes tumors, and sarcomas, and epithelial tumors such as large duct papillomas; carcinomas of the breast including in situ (noninvasive) carcinoma that includes ductal carcinoma in situ (including Paget's disease) and lobular carcinoma in situ, and invasive (infiltrating) carcinoma including, but not limited to, invasive ductal carcinoma, invasive lobular carcinoma, medullary carcinoma, colloid (mucinous) carcinoma, tubular carcinoma, and invasive papillary carcinoma; and miscellaneous malignant neoplasms. Further examples of breast cancers can include luminal A, luminal B, basal A, basal B, and triple negative breast cancer, which is estrogen receptor negative (ER^-), progesterone receptor negative, and her2 negative ($her2^-$). In some embodiments, the breast cancer may have a high risk Oncotype score.

2) Cardiac cancers, including, for example sarcoma, e.g., angiosarcoma, fibrosarcoma, rhabdomyosarcoma, and liposarcoma; myxoma; rhabdomyoma; fibroma; lipoma and teratoma.

3) Lung cancers, including, for example, bronchogenic carcinoma, e.g., squamous cell, undifferentiated small cell, undifferentiated large cell, and adenocarcinoma; alveolar and bronchiolar carcinoma; bronchial adenoma; sarcoma; lymphoma; chondromatous hamartoma; and mesothelioma.

4) Gastrointestinal cancer, including, for example, cancers of the esophagus, e.g., squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, and lymphoma; cancers of the stomach, e.g., carcinoma, lymphoma, and leiomyosarcoma; cancers of the pancreas, e.g., ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, and vipoma; cancers of the small bowel, e.g., adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, and fibroma; cancers of the large bowel, e.g., adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, and leiomyoma.

5) Genitourinary tract cancers, including, for example, cancers of the kidney, e.g., adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, and leukemia; cancers of the bladder and urethra, e.g., squamous cell carcinoma, transitional cell carcinoma, and adenocarcinoma; cancers of the prostate, e.g., adenocarcinoma, and sarcoma; cancer of the testis, e.g., seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, and lipoma.

6) Liver cancers, including, for example, hepatoma, e.g., hepatocellular carcinoma; cholangiocarcinoma; hepatoblastoma; angiosarcoma; hepatocellular adenoma; and hemangioma.

7) Bone cancers, including, for example, osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochrondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors.

8) Nervous system cancers, including, for example, cancers of the skull, e.g., osteoma, hemangioma, granuloma, xanthoma, and osteitis deformans; cancers of the meninges, e.g., meningioma, meningiosarcoma, and gliomatosis; cancers of the brain, e.g., astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, and congenital tumors; and cancers of the spinal cord, e.g., neurofibroma, meningioma, glioma, and sarcoma.

9) Gynecological cancers, including, for example, cancers of the uterus, e.g., endometrial carcinoma; cancers of the cervix, e.g., cervical carcinoma, and pre tumor cervical dysplasia; cancers of the ovaries, e.g., ovarian carcinoma, including serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma, granulosa theca cell tumors, Sertoli Leydig cell tumors, dysgerminoma, and malignant teratoma; cancers of the vulva, e.g., squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, and melanoma; cancers of the vagina, e.g., clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, and embryonal rhabdomyosarcoma; and cancers of the fallopian tubes, e.g., carcinoma.

10) Hematologic cancers, including, for example, cancers of the blood, e.g., acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, and myelodysplastic syndrome, Hodgkin's lymphoma, non-Hodgkin's lymphoma (malignant lymphoma) and Waldenstrim's macroglobulinemia.

11) Skin cancers and skin disorders, including, for example, malignant melanoma and metastatic melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, and scleroderma.

12) Adrenal gland cancers, including, for example, neuroblastoma.

Cancers may be solid tumors that may or may not be metastatic. Cancers may also occur, as in leukemia, as a diffuse tissue. Thus, the term "tumor cell," as provided herein, includes a cell afflicted by any one of the above identified disorders.

A method of treating cancer using a compound or composition as described herein may be combined with existing methods of treating cancers, for example by chemotherapy, irradiation, or surgery (e.g., oophorectomy). In some embodiments, a compound or composition can be administered before, during, or after another anticancer agent or treatment.

The compounds and compositions described herein can be used as anti-angiogenesis agents and as agents for modulating and/or inhibiting the activity of protein kinases, thus providing treatments for cancer and other diseases associated with cellular proliferation mediated by protein kinases. For example, the compounds described herein can inhibit the activity of one or more kinases. Accordingly, provided herein is a method of treating cancer or preventing or reducing angiogenesis through kinase inhibition.

In addition, and including treatment of cancer, the compounds and compositions described herein can function as cell-cycle control agents for treating proliferative disorders in a patient. Disorders associated with excessive proliferation include, for example, cancers, scleroderma, immuno-

logical disorders involving undesired proliferation of leukocytes, and restenosis and other smooth muscle disorders. Furthermore, such compounds may be used to prevent de-differentiation of post-mitotic tissue and/or cells.

Diseases or disorders associated with uncontrolled or abnormal cellular proliferation include, but are not limited to, the following:

- a variety of cancers, including, but not limited to, carcinoma, hematopoietic tumors of lymphoid lineage, hematopoietic tumors of myeloid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system and other tumors including melanoma, seminoma and Kaposi's sarcoma.
- a disease process which features abnormal cellular proliferation, e.g., benign prostatic hyperplasia, familial adenomatosis polyposis, neurofibromatosis, atherosclerosis, arthritis, glomerulonephritis, restenosis following angioplasty or vascular surgery, inflammatory bowel disease, transplantation rejection, endotoxic shock, and fungal infections. Fibrotic disorders such as skin fibrosis; scleroderma; progressive systemic fibrosis; lung fibrosis; muscle fibrosis; kidney fibrosis; glomerulosclerosis; glomerulonephritis; hypertrophic scar formation; uterine fibrosis; renal fibrosis; cirrhosis of the liver, liver fibrosis; fatty liver disease (FLD); adhesions, such as those occurring in the abdomen, pelvis, spine or tendons; chronic obstructive pulmonary disease; fibrosis following myocardial infarction; pulmonary fibrosis; fibrosis and scarring associated with diffuse/interstitial lung disease; central nervous system fibrosis, such as fibrosis following stroke; fibrosis associated with neuro-degenerative disorders such as Alzheimer's Disease or multiple sclerosis; fibrosis associated with proliferative vitreoretinopathy (PVR); restenosis; endometriosis; ischemic disease and radiation fibrosis.
- defective apoptosis-associated conditions, such as cancers (including but not limited to those types mentioned herein), viral infections (including but not limited to herpesvirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus), prevention of AIDS development in HIV-infected individuals, autoimmune diseases (including but not limited to systemic lupus erythematosus, rheumatoid arthritis, sepsis, ankylosing spondylitis, psoriasis, scleroderma, autoimmune mediated glomerulonephritis, inflammatory bowel disease and autoimmune diabetes mellitus), neuro-degenerative disorders (including but not limited to Alzheimer's disease, lung disease, amyotrophic lateral sclerosis, retinitis pigmentosa, Parkinson's disease, AIDS-related dementia, spinal muscular atrophy and cerebellar degeneration), myelodysplastic syndromes, aplastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (including but not limited to chronic anemia and aplastic anemia), degenerative diseases of the musculoskeletal system (including but not limited to osteoporosis and arthritis), tendinopathies such as tendinitis and tendinosis, aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain.
- genetic diseases due to mutations in Wnt signaling components, such as polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects and/or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

The compounds and compositions described herein can be used to treat neurological conditions, disorders and/or diseases caused by dysfunction in the Wnt signaling pathway. Non-limiting examples of neurological conditions/disorders/diseases which can be treated with the compounds and compositions provided herein include Alzheimer's disease, aphasia, apraxia, arachnoiditis, ataxia telangiectasia, attention deficit hyperactivity disorder, auditory processing disorder, autism, alcoholism, Bell's palsy, bipolar disorder, brachial plexus injury, Canavan disease, carpal tunnel syndrome, causalgia, central pain syndrome, central pontine myelinolysis, centronuclear myopathy, cephalic disorder, cerebral aneurysm, cerebral arteriosclerosis, cerebral atrophy, cerebral gigantism, cerebral palsy, cerebral vasculitis, cervical spinal stenosis, Charcot-Marie-Tooth disease, Chiari malformation, chronic fatigue syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic pain, Coffin-Lowry syndrome, complex regional pain syndrome, compression neuropathy, congenital facial diplegia, corticobasal degeneration, cranial arteritis, craniosynostosis, Creutzfeldt-Jakob disease, cumulative trauma disorder, Cushing's syndrome, cytomegalic inclusion body disease (CIBD), Dandy-Walker syndrome, Dawson disease, de Morsier's syndrome, Dejerine-Klumpke palsy, Dejerine-Sottas disease, delayed sleep phase syndrome, dementia, dermatomyositis, developmental dyspraxia, diabetic neuropathy, diffuse sclerosis, Dravet syndrome, dysautonomia, dyscalculia, dysgraphia, dyslexia, dystonia, empty sella syndrome, encephalitis, encephalocele, encephalotrigeminal angiomatosis, encopresis, epilepsy, Erb's palsy, erythromelalgia, essential tremor, Fabry's disease, Fahr's syndrome, familial spastic paralysis, febrile seizure, Fisher syndrome, Friedreich's ataxia, fibromyalgia, Foville's syndrome, Gaucher's disease, Gerstmann's syndrome, giant cell arteritis, giant cell inclusion disease, globoid cell leukodystrophy, gray matter heterotopia, Guillain-Barre syndrome, HTLV-1 associated myelopathy, Hallervorden-Spatz disease, hemifacial spasm, hereditary spastic paraplegia, heredopathia atactica polyneuritiformis, herpes zoster oticus, herpes zoster, Hirayama syndrome, holoprosencephaly, Huntington's disease, hydranencephaly, hydrocephalus, hypercortisolism, hypoxia, immune-mediated encephalomyelitis, inclusion body myositis, incontinentia pigmenti, infantile phytanic acid storage disease, infantile Refsum disease, infantile spasms, inflammatory myopathy, intracranial cyst, intracranial hypertension, Joubert syndrome, Karak syndrome, Kearns-Sayre syndrome, Kennedy disease, Kinsbourne syndrome, Klippel Feil syndrome, Krabbe disease, Kugelberg-Welander disease, kuru, Lafora disease, Lambert-Eaton myasthenic syndrome, Landau-Kleffner syndrome, lateral medullary (Wallenberg) syndrome, Leigh's disease, Lennox-Gastaut syndrome, Lesch-Nyhan syndrome, leukodystrophy, Lewy body dementia, lissencephaly,

locked-in syndrome, Lou Gehrig's disease, lumbar disc disease, lumbar spinal stenosis, Lyme disease, Machado-Joseph disease (Spinocerebellar ataxia type 3), macrencephaly, macropsia, megalencephaly, Melkersson-Rosenthal syndrome, Meniere's disease, meningitis, Menkes disease, metachromatic leukodystrophy, microcephaly, micropsia, Miller Fisher syndrome, misophonia, mitochondrial myopathy, Mobius syndrome, monomelic amyotrophy, motor neuron disease, motor skills disorder, Moyamoya disease, mucopolysaccharidoses, multi-infarct dementia, multifocal motor neuropathy, multiple sclerosis, multiple system atrophy, muscular dystrophy, myalgic encephalomyelitis, myasthenia gravis, myelinoclastic diffuse sclerosis, myoclonic Encephalopathy of infants, myoclonus, myopathy, myotubular myopathy, myotonia congenital, narcolepsy, neurofibromatosis, neuroleptic malignant syndrome, lupus erythematosus, neuromyotonia, neuronal ceroid lipofuscinosis, Niemann-Pick disease, O'Sullivan-McLeod syndrome, occipital Neuralgia, occult Spinal Dysraphism Sequence, Ohtahara syndrome, olivopontocerebellar atrophy, opsoclonus myoclonus syndrome, optic neuritis, orthostatic hypotension, palinopsia, paresthesia, Parkinson's disease, paramyotonia Congenita, paraneoplastic diseases, paroxysmal attacks, Parry-Romberg syndrome, Pelizaeus-Merzbacher disease, periodic paralyses, peripheral neuropathy, photic sneeze reflex, phytanic acid storage disease, Pick's disease, polymicrogyria (PMG), polymyositis, porencephaly, post-polio syndrome, postherpetic neuralgia (PHN), postural hypotension, Prader-Willi syndrome, primary lateral sclerosis, prion diseases, progressive hemifacial atrophy, progressive multifocal leukoencephalopathy, progressive supranuclear palsy, pseudotumor cerebri, Ramsay Hunt syndrome type I, Ramsay Hunt syndrome type II, Ramsay Hunt syndrome type III, Rasmussen's encephalitis, reflex neurovascular dystrophy, Refsum disease, restless legs syndrome, retrovirus-associated myelopathy, Rett syndrome, Reye's syndrome, rhythmic movement disorder, Romberg syndrome, Saint Vitus dance, Sandhoff disease, schizophrenia, Schilder's disease, schizencephaly, sensory integration dysfunction, septo-optic dysplasia, Shy-Drager syndrome, Sjögren's syndrome, snatiation, Sotos syndrome, spasticity, spina bifida, spinal cord tumors, spinal muscular atrophy, spinocerebellar ataxia, Steele-Richardson-Olszewski syndrome, Stiff-person syndrome, stroke, Sturge-Weber syndrome, subacute sclerosing panencephalitis, subcortical arteriosclerotic encephalopathy, superficial siderosis, Sydenham's chorea, syncope, synesthesia, syringomyelia, tarsal tunnel syndrome, tardive dyskinesia, tardive dysphrenia, Tarlov cyst, Tay-Sachs disease, temporal arteritis, tetanus, tethered spinal cord syndrome, Thomsen disease, thoracic outlet syndrome, tic douloureux, Todd's paralysis, Tourette syndrome, toxic encephalopathy, transient ischemic attack, transmissible spongiform encephalopathies, transverse myelitis, tremor, trigeminal neuralgia, tropical spastic paraparesis, trypanosomiasis, tuberous sclerosis, ubisiosis, Von Hippel-Lindau disease (VHL), Viliuisk Encephalomyelitis (VE), Wallenberg's syndrome, Werdnig, Hoffman disease, west syndrome, Williams syndrome, Wilson's disease and Zellweger syndrome.

The compounds and compositions may also be useful in the inhibition of the development of invasive cancer, tumor angiogenesis and metastasis.

In some embodiments, the disclosure provides a method for treating a disease or disorder associated with aberrant cellular proliferation by administering to a patient in need of such treatment an effective amount of one or more of the compounds of Formula (I), in combination (simultaneously or sequentially) with at least one other agent.

In some embodiments, the disclosure provides a method of treating or ameliorating in a patient a disorder or disease selected from the group consisting of: cancer, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), degenerative disc disease, bone/osteoporotic fractures, bone or cartilage disease, and osteoarthritis, the method comprising administering to the patient a therapeutically effective amount of a compound according to claim **1**, or a pharmaceutically acceptable salt thereof.

In some embodiments, the pharmaceutical composition comprises a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In some embodiments, the method of treats a disorder or disease in which aberrant Wnt signaling is implicated in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the disorder or disease is cancer.

In some embodiments, the disorder or disease is systemic inflammation.

In some embodiments, the disorder or disease is metastatic melanoma.

In some embodiments, the disorder or disease is fatty liver disease.

In some embodiments, the disorder or disease is liver fibrosis.

In some embodiments, the disorder or disease is tendonitis.

In some embodiments, the disorder or disease is damage to a tendon which would benefit from tendon regeneration.

In some embodiments, the disorder or disease is diabetes.

In some embodiments, the disorder or disease is degenerative disc disease.

In some embodiments, the disorder or disease is osteoarthritis.

In some embodiments, the disorder or disease is diabetic retinopathy.

In some embodiments, the disorder or disease is pulmonary fibrosis.

In some embodiments, the disorder or disease is idiopathic pulmonary fibrosis (IPF).

In some embodiments, the disorder or disease is degenerative disc disease.

In some embodiments, the disorder or disease is rheumatoid arthritis.

In some embodiments, the disorder or disease is scleroderma.

In some embodiments, the disorder or disease is a mycotic or viral infection.

In some embodiments, the disorder or disease is a bone or cartilage disease.

In some embodiments, the disorder or disease is Alzheimer's disease.

In some embodiments, the disorder or disease is osteoarthritis.

In some embodiments, the disorder or disease is lung disease

In some embodiments, the disorder or disease is a genetic disease caused by mutations in Wnt signaling components, wherein the genetic disease is selected from: polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2,

Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

In some embodiments, the patient is a human.

In some embodiments, the cancer is chosen from: hepatocellular carcinoma, colon cancer, breast cancer, pancreatic cancer, chronic myeloid leukemia (CML), chronic myelomonocytic leukemia, chronic lymphocytic leukemia (CLL), acute myeloid leukemia, acute lymphocytic leukemia, Hodgkin lymphoma, lymphoma, sarcoma and ovarian cancer.

In some embodiments, the cancer is chosen from: lung cancer—non-small cell, lung cancer—small cell, multiple myeloma, nasopharyngeal cancer, neuroblastoma, osteosarcoma, penile cancer, pituitary tumors, prostate cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, skin cancer—basal and squamous cell, skin cancer—melanoma, small intestine cancer, stomach (gastric) cancers, testicular cancer, thymus cancer, thyroid cancer, uterine sarcoma, vaginal cancer, vulvar cancer, laryngeal or hypopharyngeal cancer, kidney cancer, Kaposi sarcoma, gestational trophoblastic disease, gastrointestinal stromal tumor, gastrointestinal carcinoid tumor, gallbladder cancer, eye cancer (melanoma and lymphoma), Ewing tumor, esophagus cancer, endometrial cancer, colorectal cancer, cervical cancer, brain or spinal cord tumor, bone metastasis, bone cancer, bladder cancer, bile duct cancer, anal cancer and adrenal cortical cancer.

In some embodiments, the cancer is hepatocellular carcinoma.

In some embodiments, the cancer is colon cancer.

In some embodiments, the cancer is colorectal cancer.

In some embodiments, the cancer is breast cancer.

In some embodiments, the cancer is pancreatic cancer.

In some embodiments, the cancer is chronic myeloid leukemia (CML).

In some embodiments, the cancer is chronic myelomonocytic leukemia.

In some embodiments, the cancer is chronic lymphocytic leukemia (CLL).

In some embodiments, the cancer is acute myeloid leukemia.

In some embodiments, the cancer is acute lymphocytic leukemia.

In some embodiments, the cancer is Hodgkin lymphoma.

In some embodiments, the cancer is lymphoma.

In some embodiments, the cancer is sarcoma.

In some embodiments, the cancer is ovarian cancer.

In some embodiments, the cancer is lung cancer—non-small cell.

In some embodiments, the cancer is lung cancer—small cell.

In some embodiments, the cancer is multiple myeloma.

In some embodiments, the cancer is nasopharyngeal cancer.

In some embodiments, the cancer is neuroblastoma.

In some embodiments, the cancer is osteosarcoma.

In some embodiments, the cancer is penile cancer.

In some embodiments, the cancer is pituitary tumors.

In some embodiments, the cancer is prostate cancer.

In some embodiments, the cancer is retinoblastoma.

In some embodiments, the cancer is rhabdomyosarcoma.

In some embodiments, the cancer is salivary gland cancer.

In some embodiments, the cancer is skin cancer—basal and squamous cell.

In some embodiments, the cancer is skin cancer—melanoma.

In some embodiments, the cancer is small intestine cancer.

In some embodiments, the cancer is stomach (gastric) cancers.

In some embodiments, the cancer is testicular cancer.

In some embodiments, the cancer is thymus cancer.

In some embodiments, the cancer is thyroid cancer.

In some embodiments, the cancer is uterine sarcoma.

In some embodiments, the cancer is vaginal cancer.

In some embodiments, the cancer is vulvar cancer.

In some embodiments, the cancer is Wilms tumor.

In some embodiments, the cancer is laryngeal or hypopharyngeal cancer.

In some embodiments, the cancer is kidney cancer.

In some embodiments, the cancer is Kaposi sarcoma.

In some embodiments, the cancer is gestational trophoblastic disease.

In some embodiments, the cancer is gastrointestinal stromal tumor.

In some embodiments, the cancer is gastrointestinal carcinoid tumor.

In some embodiments, the cancer is gallbladder cancer.

In some embodiments, the cancer is eye cancer (melanoma and lymphoma).

In some embodiments, the cancer is Ewing tumor.

In some embodiments, the cancer is esophagus cancer.

In some embodiments, the cancer is endometrial cancer.

In some embodiments, the cancer is colorectal cancer.

In some embodiments, the cancer is cervical cancer.

In some embodiments, the cancer is brain or spinal cord tumor.

In some embodiments, the cancer is bone metastasis.

In some embodiments, the cancer is bone cancer.

In some embodiments, the cancer is bladder cancer.

In some embodiments, the cancer is bile duct cancer.

In some embodiments, the cancer is anal cancer.

In some embodiments, the cancer is adrenal cortical cancer.

In some embodiments, the disorder or disease is a neurological condition, disorder or disease, wherein the neurological condition/disorder/disease is selected from: Alzheimer's disease, frontotemporal dementias, dementia with lewy bodies, prion diseases, Parkinson's disease, Huntington's disease, progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, amyotrophic lateral sclerosis (ALS), inclusion body myositis, autism, degenerative myopathies, diabetic neuropathy, other metabolic neuropathies, endocrine neuropathies, orthostatic hypotension, multiple sclerosis and Charcot-Marie-Tooth disease.

In some embodiments, the compound of Formula (I) inhibits one or more proteins in the Wnt pathway.

In some embodiments, the compound of Formula (I) inhibits signaling induced by one or more Wnt proteins.

In some embodiments, the Wnt proteins are chosen from: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

In some embodiments, the method inhibits one or more proteins in the Wnt pathway, the method comprises contacting a cell with an effective amount of a compound of Formula (I).

In some embodiments, the cell is a human cell.

In some embodiments, the human cell is a cancerous cell.

In some embodiments, the cancerous cell is a colon cancer cell.

In some embodiments, the contacting is in vitro.

In some embodiments, the compound of Formula (I) inhibits a kinase activity.

In some embodiments, the method treats a disease or disorder mediated by the Wnt pathway in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of Formula (I) inhibits one or more Wnt proteins.

In some embodiments, the method treats a disease or disorder mediated by kinase activity in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the disease or disorder comprises tumor growth, cell proliferation, or angiogenesis.

In some embodiments, the method inhibits the activity of a protein kinase receptor, the method comprises contacting the receptor with an effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method treats a disease or disorder associated with aberrant cellular proliferation in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method prevents or reduces angiogenesis in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method prevents or reduces abnormal cellular proliferation in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

In some embodiments, the method treats a disease or disorder associated with aberrant cellular proliferation in a patient, the method comprises administering to the patient a pharmaceutical composition comprising one or more of the compounds of claim **1** in combination with a pharmaceutically acceptable carrier and one or more other agents.

Moreover, the compounds and compositions, for example, as inhibitors of the cyclin-dependent kinases (CDKs), can modulate the level of cellular RNA and DNA synthesis and therefore are expected to be useful in the treatment of viral infections such as HIV, human papilloma virus, herpes virus, Epstein-Barr virus, adenovirus, Sindbis virus, pox virus and the like.

Compounds and compositions described herein can inhibit the kinase activity of, for example, CDK/cyclin complexes, such as those active in the G_0. or G_1 stage of the cell cycle, e.g., CDK2, CDK4, and/or CDK6 complexes.

Evaluation of Biological Activity

The biological activity of the compounds described herein can be tested using any suitable assay known to those of skill in the art, see, e.g., WO 2001/053268 and WO 2005/009997. For example, the activity of a compound may be tested using one or more of the test methods outlined below.

In one example, tumor cells may be screened for Wnt independent growth. In such a method, tumor cells of interest are contacted with a compound (i.e. inhibitor) of interest, and the proliferation of the cells, e.g. by uptake of tritiated thymidine, is monitored. In some embodiments, tumor cells may be isolated from a candidate patient who has been screened for the presence of a cancer that is associated with a mutation in the Wnt signaling pathway. Candidate cancers include, without limitation, those listed above.

In another example, one may utilize in vitro assays for Wnt biological activity, e.g. stabilization of β-catenin and promoting growth of stem cells. Assays for biological activity of Wnt include stabilization of β-catenin, which can be measured, for example, by serial dilutions of a candidate inhibitor composition. An exemplary assay for Wnt biological activity contacts a candidate inhibitor with cells containing constitutively active Wnt/β-catenin signaling. The cells are cultured for a period of time sufficient to stabilize β-catenin, usually at least about 1 hour, and lysed. The cell lysate is resolved by SDS PAGE, then transferred to nitrocellulose and probed with antibodies specific for β-catenin.

In a further example, the activity of a candidate compound can be measured in a *Xenopus* secondary axis bioassay (Leyns, L. et al. *Cell* (1997), 88(6), 747-756).

To further illustrate this invention, the following examples are included. The examples should not, of course, be construed as specifically limiting the invention. Variations of these examples within the scope of the claims are within the purview of one skilled in the art and are considered to fall within the scope of the invention as described, and claimed herein. The reader will recognize that the skilled artisan, armed with the present disclosure, and skill in the art is able to prepare and use the invention without exhaustive examples.

EXAMPLES

Compound Preparation

The starting materials used in preparing the compounds of the invention are known, made by known methods, or are commercially available. It will be apparent to the skilled artisan that methods for preparing precursors and functionality related to the compounds claimed herein are generally described in the literature. The skilled artisan given the literature and this disclosure is well equipped to prepare any of the compounds.

It is recognized that the skilled artisan in the art of organic chemistry can readily carry out manipulations without further direction, that is, it is well within the scope and practice of the skilled artisan to carry out these manipulations. These include reduction of carbonyl compounds to their corresponding alcohols, oxidations, acylations, aromatic substitutions, both electrophilic and nucleophilic, etherifications, esterification and saponification and the like. These manipulations are discussed in standard texts such as *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure* 7th Ed., John Wiley & Sons (2013), Carey and Sundberg, *Advanced Organic Chemistry* 5th Ed., Springer (2007), *Comprehensive Organic Transformations: A Guide to Functional Group Transformations,* 2nd Ed., John Wiley & Sons (1999) (incorporated herein by reference in its entirety) and the like.

The skilled artisan will readily appreciate that certain reactions are best carried out when other functionality is

masked or protected in the molecule, thus avoiding any undesirable side reactions and/or increasing the yield of the reaction. Often the skilled artisan utilizes protecting groups to accomplish such increased yields or to avoid the undesired reactions. These reactions are found in the literature and are also well within the scope of the skilled artisan. Examples of many of these manipulations can be found for example in T. Greene and P. Wuts *Protective Groups in Organic Synthesis,* 4th Ed., John Wiley & Sons (2007), incorporated herein by reference in its entirety.

Trademarks used herein are examples only and reflect illustrative materials used at the time of the invention. The skilled artisan will recognize that variations in lot, manufacturing processes, and the like, are expected. Hence the examples, and the trademarks used in them are non-limiting, and they are not intended to be limiting, but are merely an illustration of how a skilled artisan may choose to perform one or more of the embodiments of the invention.

(^{1}H) nuclear magnetic resonance spectra (NMR) were measured in the indicated solvents on a Bruker NMR spectrometer (Avance™ DRX300, 300 MHz for ^{1}H or Avance™ DRX500, 500 MHz for ^{1}H) or Varian NMR spectrometer (Mercury 400BB, 400 MHz for ^{1}H). Peak positions are expressed in parts per million (ppm) downfield from tetramethylsilane. The peak multiplicities are denoted as follows, s, singlet; d, doublet; t, triplet; q, quartet; ABq, AB quartet; quin, quintet; sex, sextet; sep, septet; non, nonet; dd, doublet of doublets; ddd, doublet of doublets of doublets; d/ABq, doublet of AB quartet; dt, doublet of triplets; td, triplet of doublets; dq, doublet of quartets; m, multiplet.

The following abbreviations have the indicated meanings:

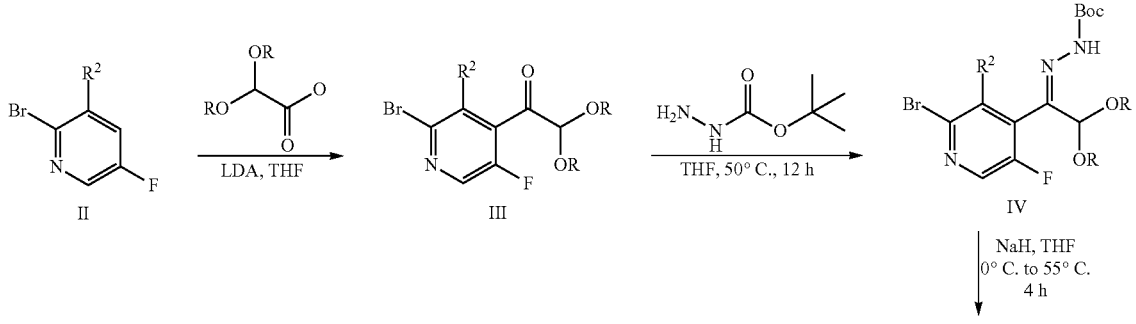
BH_3-Me_2S=borane dimethyl sulfide complex
$(Boc)_2O$=di-tert-butyl dicarbonate
brine=saturated aqueous sodium chloride
$CDCl_3$=deuterated chloroform
CD_3OD=deuterated methanol
DCAD=di-(4-chlorobenzyl)azodicarboxylate
DCE=dichloroethane
DCM=dichloromethane
DEAD=diethyl azodicarboxylate
DHP=dihydropyran
DMAP=4-dimethylaminopyridine
DMF=N,N-dimethylformamide
DMSO-d_6=deuterated dimethylsulfoxide
ESIMS=electron spray mass spectrometry
EtOAc=ethyl acetate
EtOH=ethanol
HCl=hydrochloric acid
HOAc=acetic acid
K_2CO_3=potassium carbonate
KOAc=potassium acetate
LDA=lithium diisopropylamide
LC/MS=liquid chromatography-mass spectrometry
MeOH=methanol
$MgSO_4$=magnesium sulfate
MsCl=methanesulfonyl chloride or mesyl chloride
MW=microwave
$NaBH_4$=sodium borohydride
$NaBH(OAc)_3$=sodium triacetoxyborohydride
$NaCNBH_3$=sodium cyanoborohydride
$NaHCO_3$=sodium bicarbonate
NaOH=sodium hydroxide
$Na_2S_2O_5$=sodium metabisulfite or sodium pyrosulfite
NH_4OH=ammonium hydroxide
NMR=nuclear magnetic resonance
ON=overnight
Pd/C=palladium(0) on carbon
$Pd(dppf)Cl_2$=1,1'-bis(diphenylphosphino)ferrocene]palladium(II) chloride
$Pd(PPh_3)_4$=tetrakis(triphenylphosphine)palladium(0)
$Pd(PPh_3)_2Cl_2$=bis(triphenylphosphine)palladium(II) dichloride
PE=petroleumether
Pin_2B_2=bis(pinacolato)diboron
PPh_3=triphenylphosphine
PPTS=pyridinium p-toluenesulfonate
r.t.=room temperature
SEM-Cl=2-(trimethylsilyl)ethoxymethyl chloride
TEA=triethylamine
TFA=trifluoroacetic acid
THF=tetrahydrofuran
THP=tetrahydropyran
TLC=thin layer chromatography
p-TsOH=p-toluenesulfonic acid

The following example schemes are provided for the guidance of the reader, and collectively represent an example method for making the compounds provided herein. Furthermore, other methods for preparing compounds of the invention will be readily apparent to the person of ordinary skill in the art in light of the following reaction schemes and examples. The skilled artisan is thoroughly equipped to prepare these compounds by those methods given the literature and this disclosure. The compound numberings used in the synthetic schemes depicted below are meant for those specific schemes only, and should not be construed as or confused with same numberings in other sections of the application. Unless otherwise indicated, all variables are as defined above.

General Procedure

Compounds of Formula (I) of the present invention can be prepared as depicted in Scheme 1.

Scheme 1



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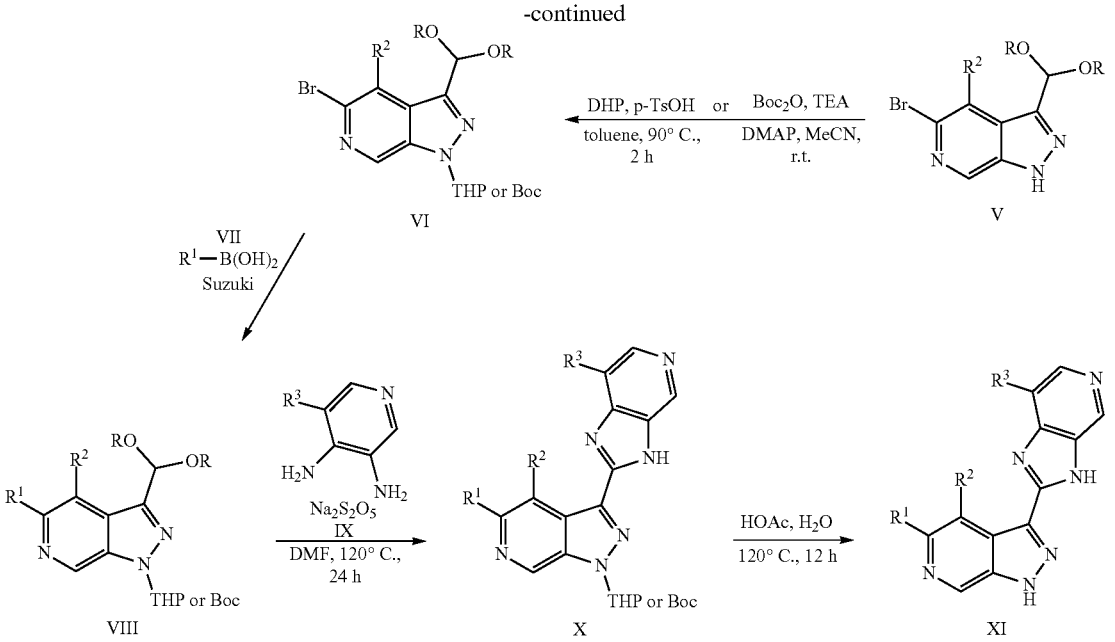
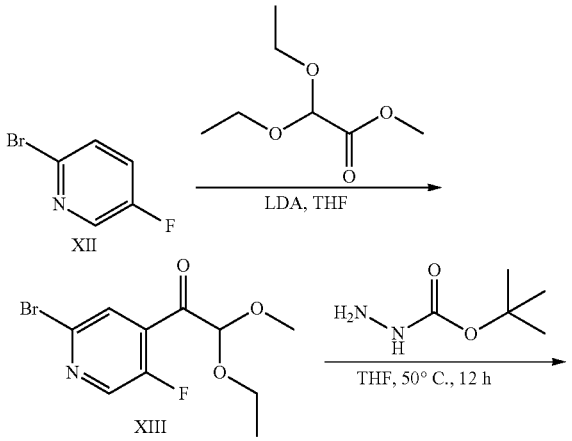


Scheme 1 describes an alternative method for preparation of 1H-pyrazolo[3,4-c]pyridine derivatives (XI) by first acylating a 2-bromo-5-fluoropyridine (II) with an ethyl 2,2-dialkoxyacetate to produce the acetal protected oxoacetaldehyde (III). The keto group was then converted to the Boc-protected hydrazone (IV) followed by base cyclization to the 1H-pyrazolo[3,4-c]pyridine (V). The pyrazolopyridine (V) is then protected with either a Boc or THP (VI) followed by Suzuki coupling with various boronic acids (VII). The pyrazolopyridine acetyl (VIII) is reacted with various 1,2-diamines (IX) to produce (X). Final deprotection of the pyrazole nitrogen yields the desired 1H-pyrazolo[3,4-c]pyridine derivatives (XI).

Illustrative Compound Examples

Preparation of Boc-protected intermediate (XVI) is depicted below in Scheme 2.

Scheme 2



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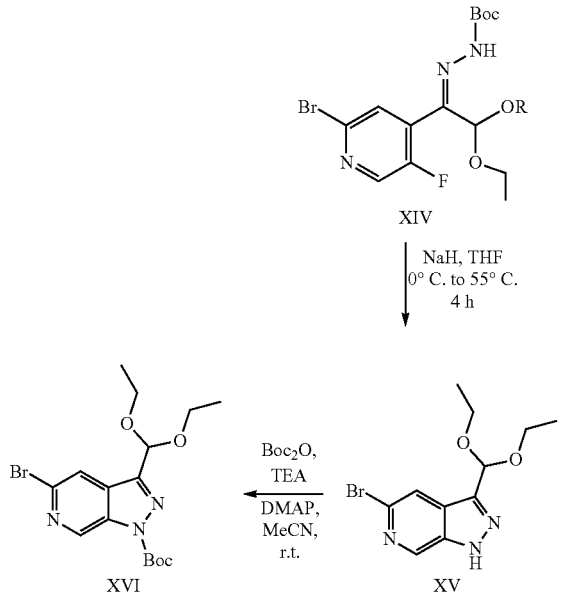


Step 1

To a solution of 2-bromo-5-fluoro-pyridine (XII) (100.0 g, 568.21 mmol, 1.0 eq) in THF (1000 mL) was added a solution of LDA (66.95 g, 625.04 mmol, 1.10 eq) drop-wise at −78° C. over a period of 1 h under N_2. The reaction mixture was stirred at −78° C. for 30 min. Then a solution of ethyl 2,2-diethoxyacetate (120.15 g, 681.86 mmol, 1.20 eq) was added at −78° C. over a period of 1 h. The reaction mixture was stirred at −78° C. for another 1 h. TLC (PE:EtOAc=10:1) showed that the starting material was consumed completely. The reaction was quenched by NH_4Cl slowly and then extracted with EtOAc (1000 mL×2). The combined organic phase was washed with saturated brine

(500 mL×2), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by chromatography on silica gel (PE:EtOAc=10:1) to give 1-(2-bromo-5-fluoropyridin-4-yl)-2,2-diethoxyethan-1-one (XIII) (160.0 g, 522.65 mmol, 92.0% yield) as a yellow solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.26 (t, J=6.8 Hz, 6H), 3.69 (q, J=7.2 Hz, 2H), 3.79 (q, J=7.2 Hz, 2H), 5.23 (d, J=2 Hz, 1H), 7.85 (d, J=4.8 Hz, 1H), 8.39 (d, J=1.2 Hz, 1H); ESIMS found for $C_{11}H_{13}BrFNO_3$ m/z 306.1 (M+H).

Step 2

To a mixture of 1-(2-bromo-5-fluoropyridin-4-yl)-2,2-diethoxyethan-1-one (XIII) (142.0 g, 463.86 mmol, 1.0 eq) in THF (2 L) tert-butyl hydrazinecarboxylate (61.30 g, 463.86 mmol, 1.0 eq) in one portion at room temperature. The mixture was stirred at 55° C. for 60 h. TLC (PE:EtOAc=2:1) showed that most of the starting material was consumed. The crude mixture of tert-butyl 2-(1-(2-bromo-5-fluoropyridin-4-yl)-2,2-diethoxyethylidene)hydrazine-1-carboxylate (XIV) was used in the next step without further purification.

Step 3

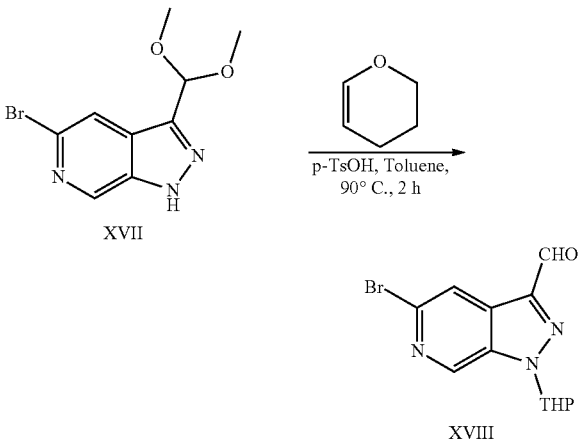
To a solution of tert-butyl 2-(1-(2-bromo-5-fluoropyridin-4-yl)-2,2-diethoxyethylidene)hydrazine-1-carboxylate (XIV) (190.0 g, 452.09 mmol, 1.0 eq) in THF (2 L) was added NaH (36.17 g, 904.18 mmol, 2.0 eq) in portions at 0° C. over 0.5 h. The mixture was stirred at 55° C. for 4 hours. TLC (PE:EtOAc=2:1) showed the material was consumed completely. The mixture was cooled to 0° C. The mixture was poured into 10% aqueous NH_4Cl (1000 mL). The aqueous phase was extracted with EtOAc (800 mL×3). The combined organic phase was washed with saturated brine (800 mL), dried with anhydrous Na_2SO_4, filtered and concentrated in vacuum. The residue was purified by silica gel chromatography (PE/EtOAc=10:1-5:1-1:4) to afford 5-bromo-3-(diethoxymethyl)-1H-pyrazolo[3,4-c]pyridine (XV) (67.0 g, 223.22 mmol, 49.4% yield) as yellow solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.30 (t, J=7.03 Hz, 6H), 3.60-3.86 (m, 4H), 5.98 (s, 1H), 8.12 (d, J=1.13 Hz, 1H), 8.96 (s, 1H), 11.82 (brs, 1H); ESIMS found for $C_{11}H_{14}BrN_3O_2$ m/z 300.0 (M+H).

Step 4

To a solution of 5-bromo-3-(diethoxymethyl)-1H-pyrazolo[3,4-c]pyridine (XV) (20.0 g, 66.63 mmol, 1.0 eq) in CH_3CN (100 mL) was added Boc_2O (21.81 g, 99.95 mmol, 1.5 eq), DMAP (814.06 mg, 6.66 mmol, 0.10 eq) and TEA (13.49 g, 133.27 mmol, 2.0 eq) at room temperature. The mixture was stirred at 15° C. for 1 hr. TLC (PE:EtOAc=5:1) showed that starting the material was consumed completely. The mixture was added water (50 mL) and extracted with EtOAc (40 mL×2). The organic layers were washed with brine (60 mL) and concentrated under vacuum. The residue was purified by chromatography on silica gel (PE:EtOAc=10:1) to produce tert-butyl 5-bromo-3-(diethoxymethyl)-1H-pyrazolo[3,4-c]pyridine-1-carboxylate (XVI) (23.70 g, 59.21 mmol, 88.9% yield) as a light yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.29 (t, J=6.8 Hz, 6H), 1.75 (s, 9H), 3.60-3.71 (m, 2H), 3.75-3.87 (m, 2H), 5.79 (s, 1H), 8.14 (d, J=1.00 Hz, 1H), 9.25 (s, 1H); ESIMS found for $C_{16}H_{22}BrN_3O_4$ m/z 400.0 (M+H).

Preparation of THP protected intermediate (XVIII) is depicted below in Scheme 3.

Scheme 3

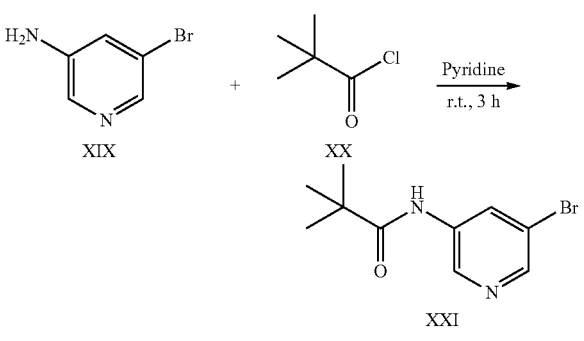


Step 1

To a mixture of 5-bromo-3-(dimethoxymethyl)-1H-pyrazolo[3,4-c]pyridine (XVII) (26.0 g, 69.85 mmol, 1.0 eq) and 3,4-dihydro-2H-pyran (14.69 g, 174.63 mmol, 2.5 eq) in toluene (100 mL) was added 4-methylbenzenesulfonic acid (2.41 g, 13.97 mmol, 0.20 eq) in one portion at room temperature under N_2. The mixture was heated to 90° C. and stirred for 2 hr. LC/MS showed the reaction was completed. the mixture was extracted with EtOAc (100 mL×3), washed with water (50 mL×2) and brine (50 mL×2). The organic layer was dried and concentrated to give a residue. the residue was purified by a column (PE:EtOAc=10:1→8:1→5:1) to give 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-c]pyridine-3-carbaldehyde (XVIII) (8.50 g, 30.65 mmol, 43.9% yield). ^1H NMR ($CDCl_3$, 500 MHz) δ ppm 1.68-1.80 (m, 2H), 1.80-1.91 (m, 1H), 2.08-2.27 (m, 2H), 2.41-2.56 (m, 1H), 3.77-3.88 (m, 1H), 3.90-4.00 (m, 1H), 5.93 (dd, J=2.8 Hz, J=8 Hz, 1H), 8.31 (s, 1H), 9.01 (s, 1H), 10.24 (s, 1H); ESIMS found $C_{12}H_{12}BrN_3O_2$ m/z 310.1 (M+H).

Preparation of intermediate N-(5-bromopyridin-3-yl) pivalamide (XXI) is depicted below in Scheme 4.

Scheme 4



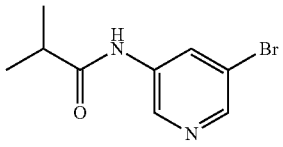
Step 1

To a solution of 3-amino-5-bromo pyridine (XIX) (1.0 g, 5.78 mmol) in dry pyridine (10 mL) was added pivaloyl chloride (XX) (769 mg, 6.38 mmol). The reaction mixture was stirred at room temperature for 3 h. The reaction was poured into an ice water/saturated aqueous $NaHCO_3$ mixture and stirred for 30 min. The precipitate was filtered, washed

with cold water and dried at room temperature to yield N-(5-bromopyridin-3-yl)pivalamide (XXI) as an off-white solid (1.082 g, 4.22 mmol, 73.1% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.23 (s, 9H), 8.37 (d, J=2 Hz, 1H), 8.39 (t, J=2 Hz, 1H), 8.80 (d, J=2 Hz, 1H), 9.58 (brs, 1H); ESIMS found $C_{10}H_{13}BrN_2O$ m/z 258.9 (Br^{81}M+H).

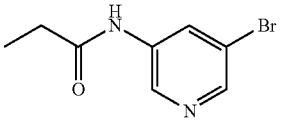
The following intermediates were prepared in accordance with the procedure described in the above Scheme 4.

XXII



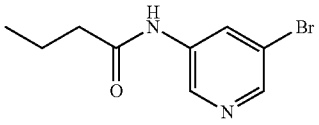
N-(5-Bromopyridin-3-yl)isobutyramide (XXII): Off-white solid, (71% yield). ^{1}H NMR ($CDCl_3$) δ ppm 8.55-8.35 (m, 3H), 7.32 (s, 1H), 2.59-2.48 (m, 1H), 1.28-1.27 (d, 6H); ESIMS found $C_9H_{11}BrN_2O$ m/z 242.9 (Br^{79}M+H).

XXIII



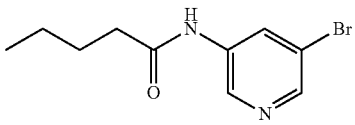
N-(5-Bromopyridin-3-yl)propionamide (XXIII): Off white solid (92% yield). ^{1}H NMR (DMSO-d_6) δ ppm 1.09 (t, J=7.54 Hz, 3H), 2.36 (q, J=7.54 Hz, 2H), 8.36 (m, 2H), 8.65 (d, J=2.07 Hz, 1H), 10.26 (s, 1H); ESIMS found $C_8H_9BrN_2O$ m/z 231.1 (Br^{81}M+H).

XXIV



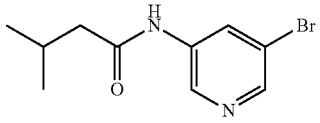
N-(5-Bromopyridin-3-yl)butyramide (XXIV): Yellow solid (2.1 g, 8.64 mmol, 88.8% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.02 (t, J=7.2 Hz, 3H), 1.74 (sxt, J=7.2 Hz, 2H), 2.40 (t, J=7.2 Hz, 2H), 8.35 (d, J=2 Hz, 1H), 8.46 (t, J=2 Hz, 1H), 8.63 (d, J=2 Hz, 1H); ESIMS found $C_9H_{11}BrN_2O$ m/z 243.1 (Br^{79}M+H).

XXV



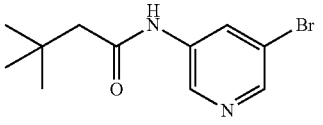
N-(5-Bromopyridin-3-yl)pentanamide (XXV): Yellow solid (2.0 g, 7.78 mmol, 85.3% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 0.98 (t, J=7.4 Hz, 3H), 1.43 (sxt, J=7.4 Hz, 2H), 1.70 (quin, J=7.4 Hz, 2H), 2.43 (t, J=7.6 Hz, 2H), 8.35 (s, 1H), 8.45 (d, J=2 Hz, 1H), 8.64 (d, J=2 Hz, 1H); ESIMS found $C_{10}H_{13}BrN_2O$ m/z 256.9 (Br^{79}M+H).

XXVI



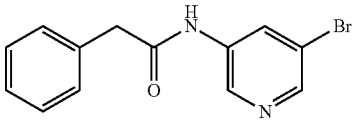
N-(5-Bromopyridin-3-yl)-3-methylbutanamide (XXVI): Off white solid, (67% yield), ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 8.55-8.42 (m, 3H), 7.62 (s, 1H), 2.31-2.18 (m, 3H), 1.02-1.01 (d, J=6 Hz, 6H); ESIMS found $C_{10}H_{13}BrN_2O$ m/z 258.9 (Br^{81}M+H).

XXVII



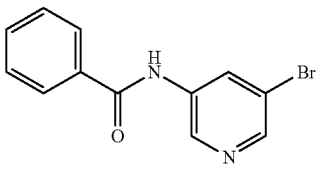
N-(5-Bromopyridin-3-yl)-3,3-dimethylbutanamide (XXVII): Yellow solid (1.7 g, 6.27 mmol, 78.6% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.10 (s, 9H), 2.29 (s, 2H), 8.36 (d, J=1.6 Hz, 1H), 8.46 (d, J=2.0 Hz, 1H), 8.64 (d, J=2.0 Hz, 1H); ESIMS found $C_{11}H_{15}BrN_2O$ m/z 273.1 ((Br^{81}M+H).

XXVIII



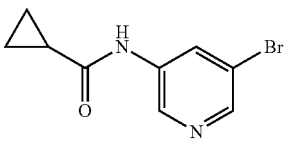
N-(5-Bromopyridin-3-yl)-2-phenylacetamide (XXVIII): White solid (2.5 g, 8.59 mmol, 77.9% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.76 (s, 2H), 7.26-7.45 (m, 5H), 7.57 (brs, 1H), 8.33 (s, 1H), 8.37 (s, 2H); ESIMS found $C_{13}H_{11}BrN_2O$ m/z 292.8 (Br^{81}M+H).

XXIX



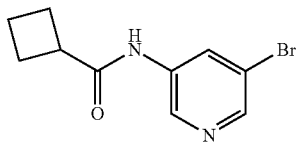
N-(5-Bromopyridin-3-yl)benzamide (XXIX): White solid (2.7 g, 9.74 mmol, 60% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.40-7.52 (m, 2H), 7.52-7.62 (m, 1H), 7.86 (d, J=7.2 Hz, 2H), 8.39 (d, J=1.6 Hz, 1H), 8.46 (s, 1H), 8.55 (d, J=1.6 Hz, 1H), 8.57 (d, J=2.0 Hz, 1H); ESIMS found $C_{12}H_9BrN_2O$ m/z 278.8 (Br^{81}M+H).

XXX



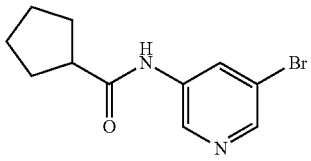
N-(5-Bromopyridin-3-yl)cyclopropanecarboxamide (XXX): Off-white solid, (83% yield), ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 8.46-8.39 (m, 3H), 7.54 (bs, 1H), 1.56-1.50 (m, 1H), 1.13-1.07 (m, 2H), 0.96-0.90 (m, 2H); ESIMS found for $C_9H_9BrN_2O$ m/z 240.9 (Br^{79}M+H).

XXXI



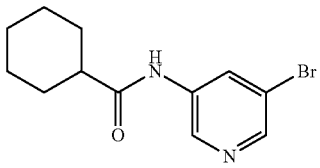
N-(5-Bromopyridin-3-yl)cyclobutanecarboxamide (XXXI): Yellow solid (2.1 g, 6.27 mmol, 86.6% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.80-1.99 (m, 1H), 1.99-2.15 (m, 1H), 2.16-2.30 (m, 2H), 2.30-2.45 (m, 2H), 3.25-3.35 (m, 1H), 8.34 (d, J=2.0 Hz, 1H), 8.47 (s, 1H), 8.64 (d, J=2.0 Hz, 1H); ESIMS found $C_{10}H_{11}BrN_2O$ m/z 257.1 (Br^{81}M+H).

XXXII



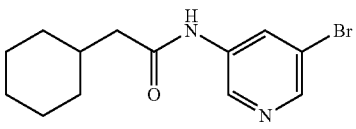
N-(5-Bromopyridin-3-yl)cyclopentanecarboxamide (XXXII): Yellow solid (1.9 g, 7.06 mmol, 80.2% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.57-1.74 (m, 2H), 1.74-1.91 (m, 4H), 1.91-2.07 (m, 2H), 2.77-2.92 (m, 1H), 8.34 (d, J=1.6 Hz, 1H), 8.45 (s, 1H), 8.65 (d, J=2.0 Hz, 1H); ESIMS found $C_{11}H_{13}BrN_2O$ m/z 271.1 (Br^{81}M+H).

XXXIII



N-(5-bromopyridin-3-yl)cyclohexanecarboxamide (XXXIII): Yellow solid (2.0 g, 7.06 mmol, 84.3% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.19-1.46 (m, 3H), 1.46-1.63 (m, 2H), 1.74 (d, J=11.6 Hz, 1H), 1.88 (t, J=14.0 Hz, 4H), 2.40 (tt, J=11.6 Hz, J=3.6 Hz, 1H), 8.34 (d, J=2.0 Hz, 1H), 8.44 (t, J=2.0 Hz, 1H), 8.64 (d, J=2.0 Hz, 1H); ESIMS found $C_{12}H_{15}BrN_2O$ m/z 285.1 (Br^{81}M+H).

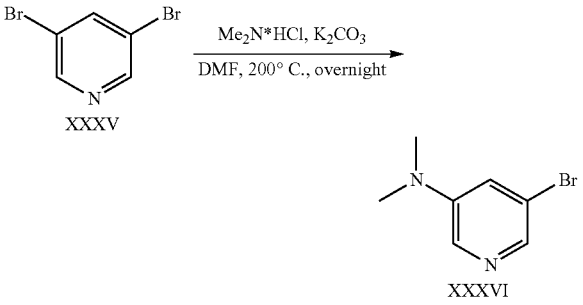
XXXIV



N-(5-bromopyridin-3-yl)-2-cyclohexylacetamide (XXXIV): Yellow solid (261 mg, 0.878 mmol, 84.4% yield). ESIMS found $C_{13}H_{17}BrN_2O$ m/z 297.1 (Br^{81}M+H).

Preparation of intermediate 5-bromo-N,N-dimethylpyridin-3-amine (XXXVI) is depicted below in Scheme 5.

Scheme 5

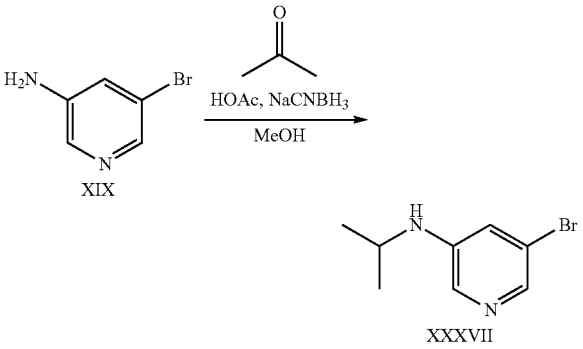


Step 1

To a solution of 3,5-dibromopyridine (XXXV) (2.37 g, 10.0 mmol) in dry DMF (20.0 mL) was added K_2CO_3 (4.5 g, 33 mmol) and dimethylamino hydrochloride (1.79 g, 22 mmol). The mixture was heated overnight at 200° C. in a sealed tube. The solution was cooled to room temperature and excess DMF was removed under vacuum. The residue was partitioned between EtOAc and water. The organic phase was separated. The aqueous phase was washed with EtOAc and the combined organic phases were dried over $MgSO_4$, and concentrated to afford 5-bromo-N,N-dimethylpyridin-3-amine (XXXVI) as an off-white solid (1.78 g, 8.85 mmol, 88% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.94 (s, 6H), 7.25 (t, J=2 Hz, 1H), 7.91 (d, J=2 Hz, 1H), 8.07 (d, J=2 Hz, 1H); ESIMS found $C_7H_9BrN_2$ m/z 201.1 (M+H).

Preparation of intermediate 5-bromo-N-isopropylpyridin-3-amine (XXXVII) is depicted below in Scheme 6.

Scheme 6



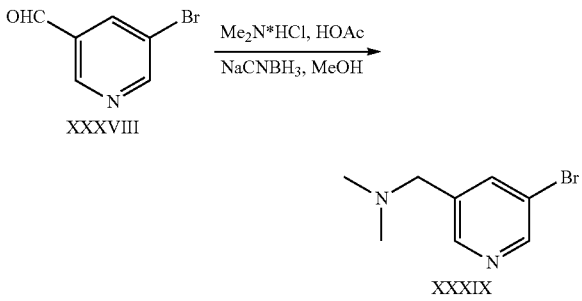
Steps 1

To a solution of 5-bromopyridin-3-amine (XIX) (535 mg, 3.09 mmol) in MeOH (62 mL) was added acetone (296 μL, 4.02 mL). The pH was adjusted to 4 using HOAc and stirred for 30 min. $NaCNBH_3$ (272 mg, 4.33 mmol) was added and stirred at room temperature overnight. The MeOH was removed under vacuum and the residue was partitioned between EtOAc and saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated under vacuum. The crude product was purified on a silica gel column (100% hexane→90:10 hexane:EtOAc) to produce 5-bromo-N-isopropylpyridin-3-amine (XXXVII) as an oil which slowly solidified into an off-white solid (309 mg, 1.44

mmol, 47% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.12 (d, J=6.3 Hz, 6H), 3.55-3.59 (m, 1H), 6.03 (d, J=7.9 Hz, 1H), 7.05-7.06 (m, 1H), 7.75 (d, J=2 Hz, 1H), 7.90 (d, J=2 Hz, 1H); ESIMS found $C_8H_{11}BrN_2$ m/z 215.1 (M+H).

Preparation of intermediate 1-(5-bromopyridin-3-yl)-N, N-dimethylmethanamine (XXXIX) is depicted below in Scheme 7.

Scheme 7

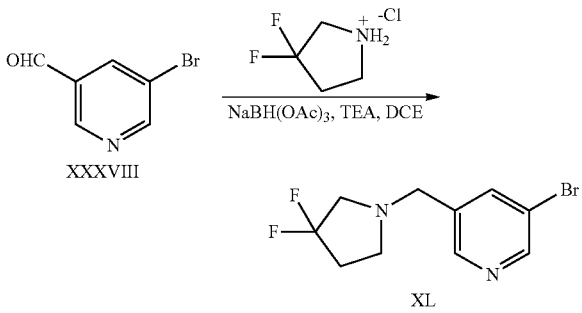


Steps 1

Preparation of 1-(5-bromopyridin-3-yl)-N,N-dimethylmethanamine (XXXIX) was performed following the procedure listed in Scheme 6, Step 1. Brown oil (1.20 g, 5.59 mmol, 45% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.15 (s, 6H), 3.43 (s, 2H), 7.94 (s, 1H), 8.47 (d, J=1.1 Hz, 1H), 8.59 (d, J=2.2 Hz, 1H); ESIMS found $C_8H_{11}BrN_2$ m/z 215 (M^{Br79}+H) and 217 (M^{Br81}+H).

Preparation of intermediate 3-bromo-5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridine (XL) is depicted below in Scheme 8.

Scheme 8

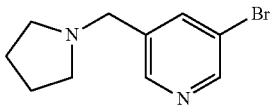


Steps 1

To a mixture of 5-bromopyridine-3-carbaldehyde (XXXVIII) (6.00 g, 32.26 mmol, 1.0 eq), 3,3-difluoropyrrolidine (5.56 g, 38.71 mmol, 1.20 eq) and TEA (5.39 mL, 38.71 mmol, 1.2 Eq) in DCE (200 mL) was stirred at room temperature for 30 min, then added sodium triacetoxyborohydride (10.25 g, 48.38 mmol, 1.50 eq) in one portion at room temperature under N_2. The mixture was stirred at room temperature for 6 hours. TLC showed the reaction was complete. The reaction was quenched with 1N NaOH (100 mL), extracted with DCE (100 mL×2). The combined organic layers were washed with brine (100 mL), dried and concentrated. The residue was purified by silica gel chromatography (column height: 50 mm, diameter: 50 mm, 300-400mesh silica gel, DCM/MeOH=30/1→20/1) to give 3-bromo-5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridine (XL): Yellow oil (8.00 g, 28.9 mmol, 89.5% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 2.30 (spt, J=7.2 Hz. 2H), 2.75 (t, J=6.8 Hz, 2H), 2.91 (t, J=13.2 Hz, 2H), 7.85 (s, 1H), 8.45 (s, 1H), 8.59 (d, J=2 Hz, 1H); ESIMS found for $C_{10}H_{11}BrF_2N_2$ m/z 277.0 (M+H).

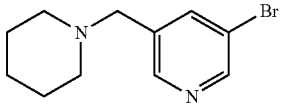
The following intermediates were prepared in accordance with the procedure described in the above Scheme 7 or Scheme 8.

XLI



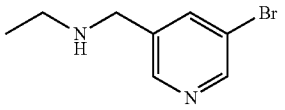
3-Bromo-5-(pyrrolidin-1-ylmethyl)pyridine (XLI): Golden liquid (1.35 g, 97% yield). H NMR (DMSO-d_6) 1.68-1.71 (m, 4H), 2.42-2.44 (m, 4H), 3.60 (s, 2H), 7.96 (s, 1H), 8.48 (d, J=2 Hz, 1H), 8.58 (d, J=Hz, 1H); ESIMS found for $C_{10}H_{13}BrN_2$ m/z 242.2 (M+H).

XLII



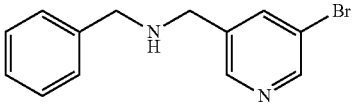
3-Bromo-5-(piperidin-1-ylmethyl)pyridine (XLII): Brown liquid (13.1 g, 94% yield). ^{1}H NMR (DMSO-d_6) 1.36-1.39 (m, 2H), 1.46-1.51 (m, 4H), 2.31-2.32 (m, 4H), 3.46 (s, 2H), 7.94 (s, 1H), 8.47 (d, J=2 Hz, 1H), 8.58 (d, J=3 Hz, 1H); ESIMS found for $C_{11}H_{15}BrN_2$ m/z

XLIII



N-((5-Bromopyridin-3-yl)methyl)ethanamine (XLIII): Golden liquid (1.29 g, 6.00 mmol, 60% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 1.14 (t, J=7.2 Hz, 3H), 2.67 (q, J=7.2 Hz, 2H), 3.79 (s, 2H), 7.85 (t, J=2 Hz, 1H), 8.46 (d, J=1.6 Hz, 1H), 8.56 (d, J=2.4 Hz, 1H); ESIMS found for $C_8H_{11}BrN_2$ m/z 215.1 (M+H).

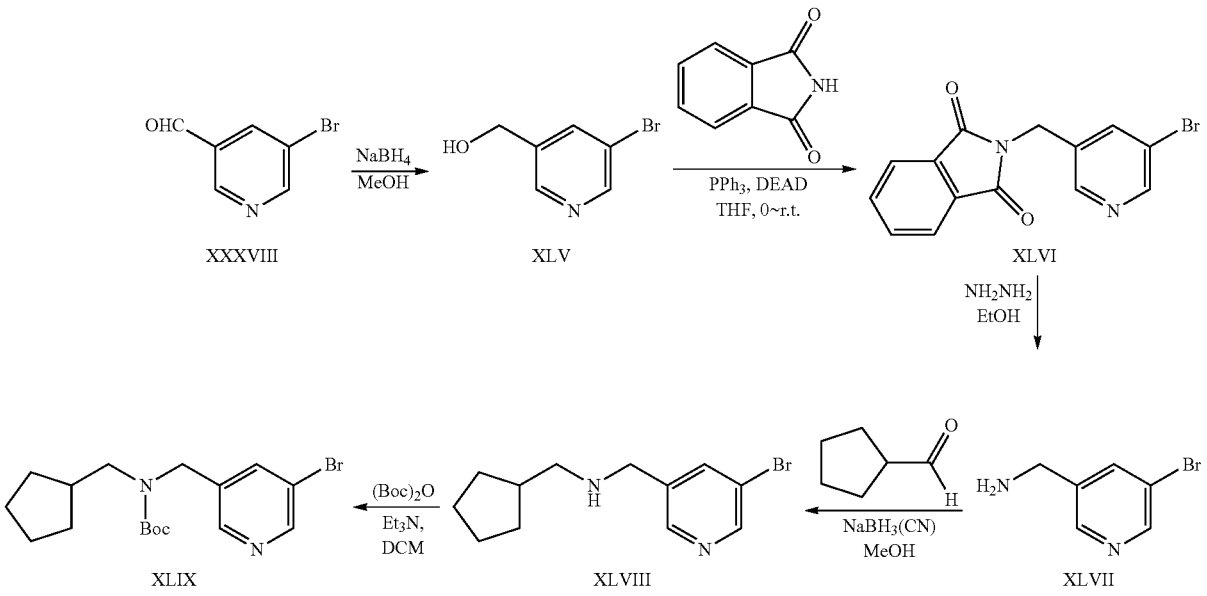
XLIV



N-Benzyl-1-(5-bromopyridin-3-yl)methanamine (XLIV): Yellow oil (8.0 g, 28.9 mmol, 89.5% yield). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.71 (s, 2H), 3.74 (s, 2H), 7.18-7.28 (m, 1H), 7.28-7.40 (m, 4H), 8.04 (s, 1H), 8.52 (s, 1H), 8.58 (s, 1H); ESIMS found for $C_{13}H_{13}BrN_2$ m/z 277.1 (M+H).

Preparation of intermediate tert-butyl (5-bromopyridin-3-yl)methyl (cyclopentylmethyl)carbamate (XLIX) is depicted below in Scheme 9.

Scheme 9



Step 1

To a solution of 5-bromonicotinaldehyde (XXXVIII) (2.0 g, 10.8 mmol, 1 eq) in MeOH (20 mL) was added $NaBH_4$ (2.4 g, 64.9 mmol, 6 eq) and the reaction mixture was stirred at room temperature for 3 h. The mixture was concentrated in vacuo and the residue was diluted in water (15 mL), the aqueous phase was extracted with DCM (10 mL×3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo to afford (5-bromopyridin-3-yl) methanol (XLV) (1.8 g, 9.57 mmol, 90.0% yield) as a colorless oil. ^1H NMR ($CDCl_3$, 500 MHz) δ ppm 4.73 (s, 2H), 7.90 (s, 1H), 8.47 (s, 1H), 8.57 (s, 1H). ESIMS found for C_6H_6BrNO m/z 188.0 (M+H).

Step 2

To a stirred solution of (5-bromopyridin-3-yl)methanol (XLV) (1.60 g, 8.5 mmol, 1 eq), phthalimide (1.24 g, 8.5 mmol, 1 eq) and PPh_3 (3.33 g, 12.75 mmol, 1.5 eq) in anhydrous THF (15 mL) was added DEAD (2.21 g, 12.75 mmol, 1.5 eq) dropwise at 0° C. under N_2. Then the reaction mixture was stirred at room temperature for 6 h. The mixture was washed with saturated $NaHCO_3$ solution (15 mL), water (15 mL) and brine (15 mL) subsequently. The organic layers were dried over $MgSO_4$, concentrated under reduced pressure, the resultant residue was purified by flash chromatography on silica gel (PE:EtOAc=4:1) to give 2-((5-bromopyridin-3-yl)methyl)isoindoline-1,3-dione (XLVI) (2.5 g, 7.88 mmol, 82.3% yield) as a white solid. ESIMS found for $C_{14}H_9BrN_2O_2$ m/z 317.1 (M+H).

Step 3

A solution of 2-((5-bromopyridin-3-yl)methyl)isoindoline-1,3-dione (XLVI) (1.9 g, 6.0 mmol, 1 eq) and hydrazine hydrate (2.0 g, 40 mmol, 6 eq) in EtOH (20 mL) was heated at 70° C. for 3 h. The mixture was filtered through a Celite® pad and the filtrate was concentrated in vacuo, the crude product was dissolved in 1N HCl solution (15 mL) and concentrated to dryness, then it was washed with acetone (10 mL×3), the precipitate was collected by filtration, dried in vacuo to give (5-bromopyridin-3-yl)methanamine (XLVII) (1.3 g, 6.95 mmol, 97.7% yield) as a white solid. ^1H NMR (D_2O, 500 MHz) δ ppm 4.34 (s, 2H), 8.56 (s, 1H), 8.75 (d, J=1.2 Hz, 1H), 8.91 (d, J=1.6 Hz, 1H). ESIMS found for $C_6H_7BrN_2$ m/z 187.0 (M+H).

Step 4

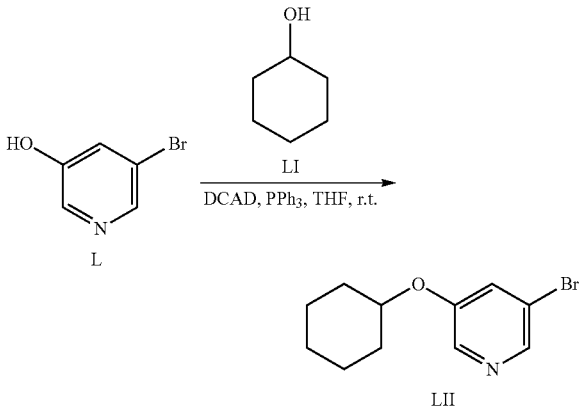
A solution of (5-bromopyridin-3-yl)methanamine (XLVII) (1.30 g, 5.8 mmol, 1.0 eq), cyclopentanecarbaldehyde (0.57 g, 5.8 mmol, 1.0 eq) and TEA (0.60 g, 5.8 mmol, 1.0 eq) in MeOH (15 mL) was stirred at room temperature for 2 h. Then $NaBH_3CN$ (1.98 g, 34.6 mmol, 6.0 eq) was added and the mixture was stirred at the same temperature for another 3 h. The solvent was removed under reduced pressure and the residue was diluted in water (20 mL) and extracted with DCM (10 mL×3), combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give 1-(5-bromopyridin-3-yl)-N-(cyclopentylmethyl)methanamine (XLVIII) (1.23 g, 4.57 mmol, 79.3% yield) as a yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.07-1.23 (m, 2H), 1.47-1.67 (m, 4H), 1.70-1.84 (m, 2H), 2.02 (spt, J=7.6 Hz. 1H), 2.53 (d, J=7.2 Hz, 2H), 3.80 (s, 2H), 7.86 (s, 1H), 8.47 (s, 1H), 8.56 (d, J=2.0 Hz, 1H); ESIMS found for $C_{12}H_{17}BrN_2$ m/z 269.1 (M+H).

Step 5

To a solution of 1-(5-bromopyridin-3-yl)-N-(cyclopentylmethyl) methanamine (XLVIII) (1.00 g, 3.7 mmol, 1 eq) and TEA (0.93 g, 9.2 mmol, 2.5 eq) in DCM (20 mL) was added portionwise $(Boc)_2O$ (0.85 g, 4.0 mmol, 1.1 eq) at 0° C., the reaction mixture was stirred at room temperature for 1 h. The mixture was washed with water (10 mL), brine (10 mL), the organic layer was separated, dried over $MgSO_4$ and concentrated in vacuo to give tert-butyl (5-bromopyridin-3-yl) methyl (cyclopentylmethyl)carbamate (XLIX) (1.25 g, 3.38 mmol, 91.9% yield) as a white solid. ESIMS found for $C_{17}H_{25}BrN_2O_2$ m/z 369.1 (M+H).

Preparation of intermediate 3-bromo-5-(cyclohexyloxy) pyridine (LII) is depicted below in Scheme 10.

Scheme 10

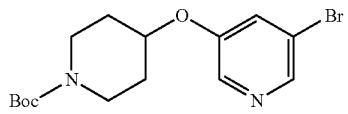


Step 1

To a solution of 5-bromopyridin-3-ol (L) (523 mg, 3.01 mmol) in THF (30 mL) cooled to 0° C. were added triphenylphosphine (867 mg, 3.31 mmol) and cyclohexanol (LI) (331 mg, 3.31 mmol) followed by (E)-bis(4-chlorobenzyl) diazene-1,2-dicarboxylate (1.21 g, 3.31 mmol), added portionwise. The reaction mixture was then stirred at 25° C. overnight. The reaction was worked-up with a EtOAc-$NaHCO_3$ extraction and the solid filtered off. The solvent was removed and the residue was purified by Isco (20% EtOAc-Hexanes) to give 3-bromo-5-(cyclohexyloxy)pyridine (LII) (209 mg, 0.82 mmol, 27.2% yield) as a yellow oil. ^1H NMR (DMSO-d_6, 500 MHz) δ ppm 1.21-1.31 (m, 1H) 1.34-1.48 (m, 4H) 1.49-1.57 (m, 1H) 1.70 (br dd, J=9.74, 4.25 Hz, 2H) 1.88-1.96 (m, 2H) 2.50 (dt, J=3.70, 1.72 Hz, 5H) 4.46-4.54 (m, 1H) 7.72 (t, J=2.20 Hz, 1H) 8.24 (d, J=1.92 Hz, 1H) 8.27 (d, J=2.47 Hz, 1H).

The following intermediate was prepared in accordance with the procedure described in the above Scheme 10.

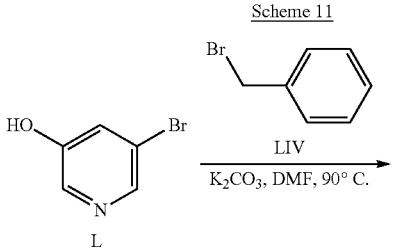
LIII



tert-Butyl 4-((5-bromopyridin-3-yl)oxy)piperidine-1-carboxylate (LIII): Yellow oil (244 mg, 0.683 mmol, 23.2% yield). ESIMS found for $C_{15}H_{21}BrN_2O_3$ m/z 358.3 (M+H).

Preparation of intermediate 3-(benzyloxy)-5-bromopyridine (LV) is depicted below in Scheme 11.

Scheme 11



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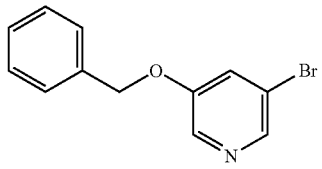


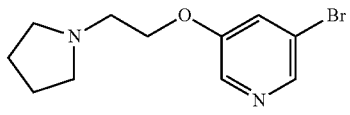
LV

Step 1

To a solution of 5-bromopyridin-3-ol (L) (174 mg, 1.0 mmol) in DMF (3 mL) was added potassium carbonate (415 mg, 3.0 mmol). The slurry was heated at 90° C. for 1 hour and then cooled to 25° C. The (bromomethyl)benzene (LIV) (171 mg, 1.0 mmol) was added and the mixture was stirred at 25° C. overnight. The reaction was worked-up using a saturated sodium bicarbonate and ethyl acetate extraction. The product was purified by ISCO column eluted with 40-100% EtOAc-Hexanes. The 3-(benzyloxy)-5-bromopyridine (LV) (105 mg, 0.398 mmol, 39.8% yield) was obtained as yellow oil. MS: 266.1. ESIMS found for $C_{12}H_{10}BrNO$ m/z 266.1 (M+H).

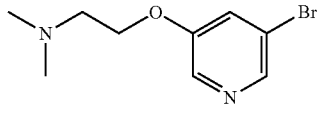
The following intermediates were prepared in accordance with the procedure described in the above Scheme 11.

LVI



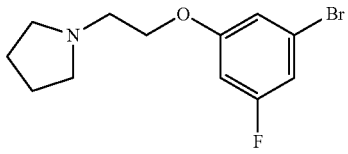
3-Bromo-5-(2-(pyrrolidin-1-yl)ethoxy)pyridine (LVI): Yellow oil ((97 mg, 0.358 mmol, 15.56% yield). ESIMS found for $C_{11}H_{15}BrN_2O$ m/z 272.2 (M+H).

LVII



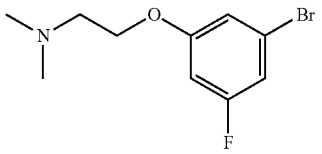
2-((5-bromopyridin-3-yl)oxy)-N,N-dimethylethan-1-amine (LVII): Yellow oil (97 mg, 0.396 mmol, 28.9% yield). ESIMS found for $C_9H_{13}BrN_2O$ m/z 245.1 (M+H).

LVIII



1-(2-(3-bromo-5-fluorophenoxy)ethyl)pyrrolidine (LVIII): Yellow oil (370 mg, 1.284 mmol, 85.8% yield). ESIMS found for $C_{12}H_{15}BrFNO$ m/z 289.0 (M+H).

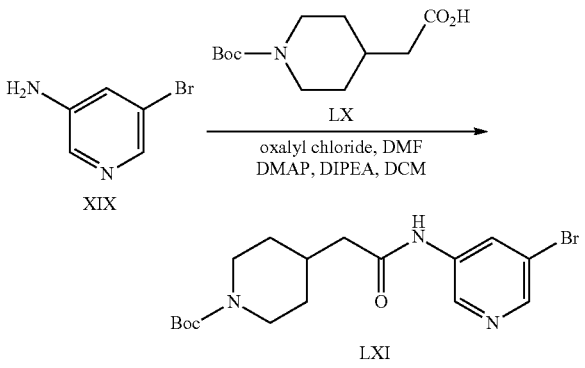
LIX



2-(3-bromo-5-fluorophenoxy)-N,N-dimethylethan-1-amine (LIX): Yellow oil (364 mg, 1.389 mmol, 50.2% yield). ESIMS found for $C_{10}H_{13}BrFNO$ m/z 263.9 (M+H).

Preparation of intermediate tert-butyl 4-(2-((5-bromopyridin-3-yl)amino)-2-oxoethyl)piperidine-1-carboxylate (LXI) is depicted below in Scheme 12.

Scheme 12

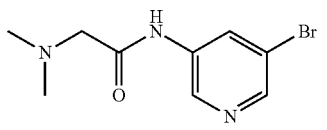


Step 1

To a solution of 2-(1-(tert-butoxycarbonyl)piperidin-4-yl) acetic acid (LX) (3.4 g, 13.97 mmol) in DCM (10 mL) was added DMF (1 mL). The solution was cooled in ice-water to 0° C. Oxalyl chloride (1.835 mL, 20.96 mmol) was then added dropwise. The mixture was stirred for one hour at 25° C. The organic volatile was then removed under vacuum. The residue was dissolved in DCM (10 mL). DMAP (0.171 g, 1.397 mmol) and 5-bromopyridin-3-amine (XIX) (2.418 g, 13.97 mmol) were added to the solution and cooled to 0° C. DIEA (4.88 ml, 27.9 mmol) was then added dropwise and the mixture was stirred for 2 hours at 25° C. The reaction was worked-up with DCM and saturated NaHCO3. The product was purified by ISCO eluted with 0-100% EtOAc-Hexanes. The tert-butyl 4-(2-((5-bromopyridin-3-yl)amino)-2-oxoethyl)piperidine-1-carboxylate (LXI) (2.82 g, 7.08 mmol, 50.7% yield) was obtained as yellow oil. ESIMS found for $C_{17}H_{24}BrN_3O_3$ m/z 343.1 (M-56).

The following intermediate was prepared in accordance with the procedure described in the above Scheme 12.

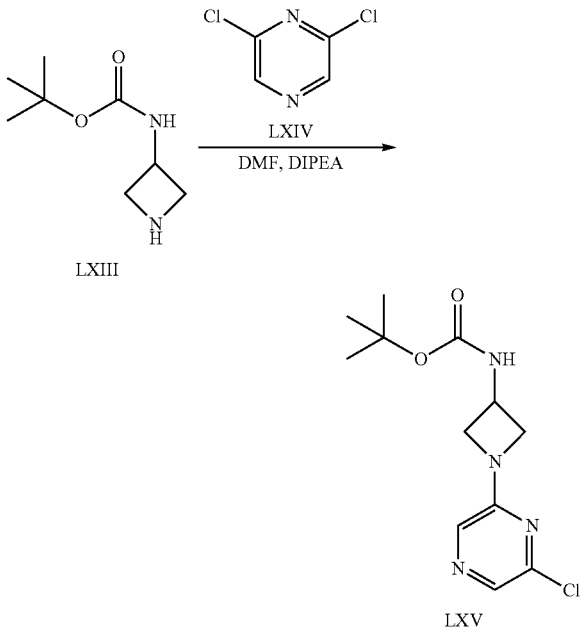
LXII



N-(5-Bromopyridin-3-yl)-2-(dimethylamino)acetamide (LXII): Yellow oil (528 mg, 2.05 mmol, 19.0% yield). ESIMS found for $C_9H_{12}BrN_3O$ m/z 259.3 (M+H).

Preparation of tert-butyl (1-(6-chloropyrazin-2-yl)azetidin-3-yl)carbamate (LXV) is depicted below in Scheme 13.

Scheme 13

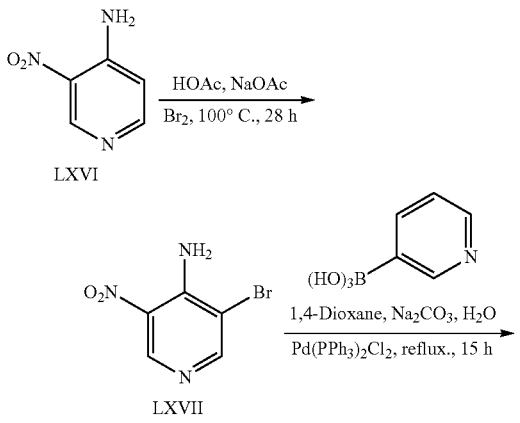


Step 1

To a solution of tert-butyl azetidin-3-ylcarbamate hydrochloride (LXIII) (2 g, 9.58 mmol) in dry DMF (19.2 mL) was added DIPEA (8.37 ml, 47.9 mmol). To this mixture was added 2,6-dichloropyrazine (LXIV) (1.428 g, 9.58 mmol) and the reaction was stirred at 95° C. for 3 hours. The reaction was quenched with water (20 mL) and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (40 g) (100% hexanes-hexanes:EtOAc 1:1) to yield tert-butyl (1-(6-chloropyrazin-2-yl)azetidin-3-yl)carbamate (LXV) (2.2882 g, 8.04 mmol, 84% yield) as a white solid. ESIMS found for $C_{12}H_{17}ClN_4O_2$ m/z 285.1 (M+H).

Preparation of intermediate [3,3'-bipyridine]-4,5-diamine (LXIX) is depicted below in Scheme 14.

Scheme 14



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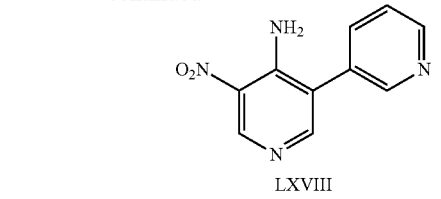
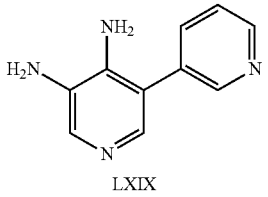


LXVIII

MeOH, Pd/C—H$_2$

rt, 15 h



LXIX

Step 1

A mixture of 3-nitropyridin-4-amine (LXVI) (10 g, 71.94 mmol) and acetic acid (120 mL) was added to a sealed tube followed by addition of NaOAc (29.50 g, 93.52 mmol) and dropwise addition of bromine (4.7 ml 359.7 mmol) under stirring. The sealed tube was heated at 100° C. for 28 h until TLC showed consumption of starting material. The reaction mixture was concentrated to obtain a solid which was dissolved in water, basified with $NaHCO_3$ and extracted with EtOAc. The combined organic extracts were dried and concentrated to produce 3-bromo-5-nitropyridin-4-amine (LXVII) as a yellow solid (12 g, 55 mmol, 77% yield). ^{1}H NMR (DMSO-d_6) δ ppm 9.19 (s, 1H), 8.58 (s, 1H); ESIMS found for $C_5H_4BrN_3O_2$ m/z 217, 219 (M+, M+2).

Step 2

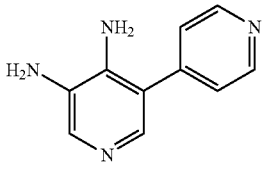
A solution of 3-bromo-5-nitropyridin-4-amine (LXVII) (6 g, 26 mmol), pyridin-3-ylboronic acid (3.54 g, 29 mmol), 1 N Na_2CO_3 solution (78 ml) and 1,4-dioxane (150 mL) was degassed with argon thrice. $Pd(PPh_3)_2Cl_2$ (927 mg, 5 mmol %) was added to the reaction and the solution was refluxed for 15 h until TLC showed the reaction was complete. The reaction was passed through a pad of Celite® and then concentrated under reduced pressure. The reaction mixture was concentrated and the residue was taken up in EtOAc. The organic extract was washed with water, dried and concentrated under vacuum. The crude product was purified on a silica gel column (100% EtOAc→2:98 MeOH:DCM) to give 5-nitro-3,3'-bipyridin-4-amine (LXVIII) as a yellow solid (5 g, 23.1 mmol, 87% yield). ^{1}H NMR ($CDCl_3$, 500 MHz,) δ ppm 9.31 (s, 1H), 8.80-8.79 (m, 1H), 8.70 (s, 1H), 8.23 (s, 1H), 7.80-7.73 (m, 1H), 7.52-7.48 (m, 1H). ESIMS found $C_{10}H_8N_4O_2$ m/z 216.95 (M+H).

Step 3

To a solution of 5-nitro-3,3'-bipyridin-4-amine (LXVIII) (5 g, 23 mmol) in MeOH (20 mL) was added 10% Pd/C. The solution was purged with hydrogen and stirred at room temperature under hydrogen for 15 h. The suspension was filtered through Celite® and the concentrated under vacuum to produce 3,3'-bipyridine-4,5-diamine (LXIX) as off white solid (3.3 g, 17.7 mmol, 76% yield). ^{1}H NMR (DMSO-d6, 500 MHz,): δ ppm 8.63-8.53 (m, 1H), 7.90-7.83 (m, 1H), 7.75 (s, 1H), 7.58 (s, 1H), 7.48-7.43 (m, 2H), 6.13 (bs, 2H), 5.31 (bs, 2H). ESIMS found $C_{10}H_{10}N_4$ m/z 187.10 (M+H).

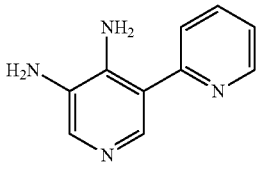
The following compounds were prepared in accordance with the procedure described in the above Scheme 14.

LXX



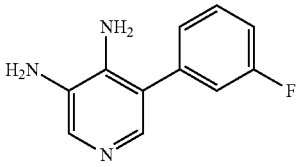
3,4'-Bipyridine-4,5-diamine (LXX): Light tan solid, (84% yield). ESIMS found $C_{10}H_{10}N_4$ m/z 187.0 (M+H).

LXXI



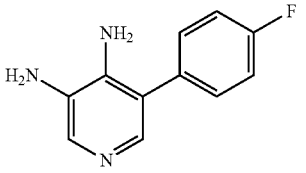
2,3'-Bipyridine-4',5'-diamine (LXXI): Tan amorphous solid, (76% yield). ESIMS found $C_{10}H_{10}N_4$ m/z 187.0 (M+H).

LXXII



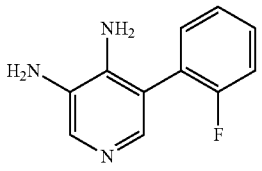
5-(3-Fluorophenyl)pyridine-3,4-diamine (LXXII): Off white solid, (76% yield), ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 4.72 (s, 2H), 5.07 (s, 2H), 7.17-7.23 (m, 3H), 7.44 (s, 1H), 7.48-7.52 (m, 1H), 7.68 (s, 1H); ESIMS found $C_{11}H_{10}FN_3$ m/z 204.1 (M+H).

LXXIII



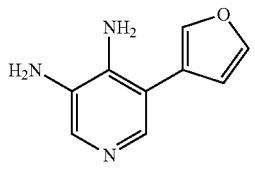
5-(4-Fluorophenyl)pyridine-3,4-diamine (LXXIII): Light yellow solid, (97% yield). ESIMS found $C_{11}H_{10}FN_3$ m/z 204.3 (M+H).

LXXIV



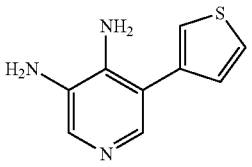
5-(2-Fluorophenyl)pyridine-3,4-diamine (LXXIV): Light red solid, (44% yield). ESIMS found $C_1H_{10}FN_3$ m/z 204.4 (M+H).

LXXV



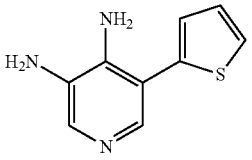
5-(Furan-3-yl)pyridine-3,4-diamine (LXXV): Light pink solid, (68% yield). ESIMS found $C_9H_9N_3O$ m/z 176.0 (M+H).

LXXVI



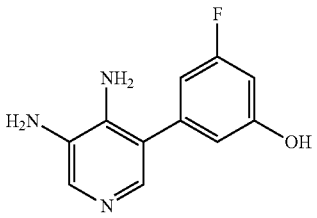
5-(Thiophen-3-yl)pyridine-3,4-diamine (LXXVI): Light brown amorphous solid, (100% yield). ESIMS found $C_9H_9N_3S$ m/z 192.0 (M+H).

LXXVII



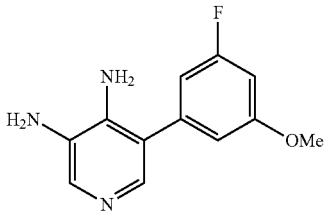
5-(thiophen-2-yl)pyridine-3,4-diamine (LXXVII): White amorphous solid, (1.257 g, 6.57 mmol, 100% yield). ESIMS found $C_9H_9N_3S$ m/z 192.2 (M+H).

LXXVIII



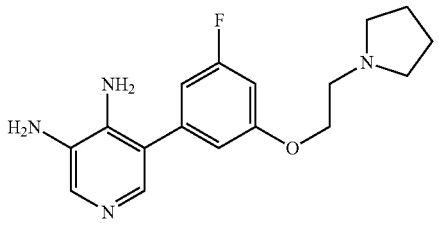
3-(4,5-Diaminopyridin-3-yl)-5-fluorophenol (LXXVIII): Yellow solid (216 mg, 0.985 mmol, 49.7% yield). ESIMS found for $C_{11}H_{10}FN_3O$ m/z 220.1 (M+H).

LXXIX



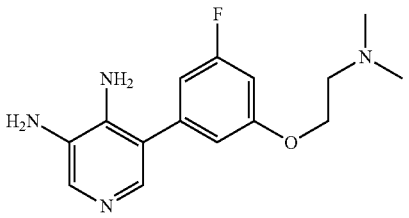
5-(3-Fluoro-5-methoxyphenyl)pyridine-3,4-diamine (LXXIX): Yellow oil (216 mg, 0.926 mmol, 81.2% yield). ESIMS found for $C_{12}H_{12}FN_3O$ m/z 234.1 (M+H

LXXX



5-(3-Fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)pyridine-3,4-diamine (LXXX): Yellow oil (94 mg, 0.297 mmol, 75.0% yield). ESIMS found for $C_{17}H_{21}FN_4O$ m/z 317.1 (M+H).

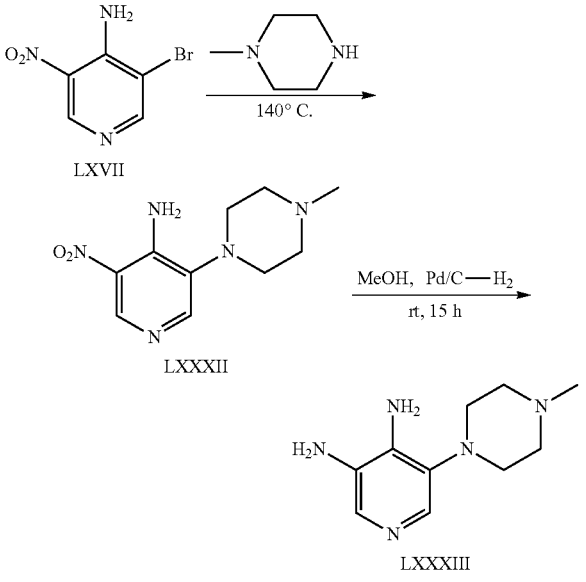
LXXXI



5-(3-(2-(Dimethylamino)ethoxy)-5-fluorophenyl)pyridine-3,4-diamine (LXXXI): Yellow solid (200 mg, 0.689 mmol, 70.5% yield). ^1H NMR (DMSO-d_6, 400 MHz); ESIMS found for $C_{15}H_{19}FN_4O$ m/z 291.1 (M+H).

Preparation of intermediate 5-(4-methylpiperazin-1-yl) pyridine-3,4-diamine (LXXXIII) is depicted below in Scheme 15.

Scheme 15



Step 1

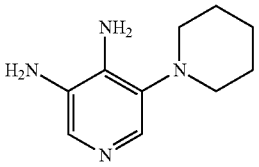
A solution of 3-bromo-5-nitropyridin-4-amine (LXVII) (618 mg, 2.83 mmol) in 1-methylpiperazine (1 mL, 8.51 mmol) was heated at 140° C. overnight. The reaction was poured into an EtOAc/H_2O mixture; the organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum. The crude product was purified on a silica gel column (100% $CHCl_3$→3:97 MeOH(7N NH_3):$CHCl_3$) to give 3-(4-methylpiperazin-1-yl)-5-nitropyridin-4-amine (LXXXII) as a yellow solid (382 mg, 1.61 mmol, 56.7% yield). ^1H NMR ($CDCl_3$, 500 MHz,) δ ppm 2.20 (s, 3H), 2.35-2.37 (m, 4H), 4.52-3.54 (m, 4H), 5.96 (s, 1H), 7.42 (s, 2H), 8.78 (s, 1H); ESIMS found $C_{10}H_{15}N_5O_2$ m/z 238 (M+H).

Step 2

To a solution of 3-(4-methylpiperazin-1-yl)-5-nitropyridin-4-amine (LXXXII) (382 mg, 1.61 mmol) in MeOH (11 mL) was added 10% Pd/C. The solution was purged with hydrogen and stirred at room temperature under hydrogen for 4 h. The suspension was filtered through Celite® and the concentrated under vacuum to produce 5-(4-methylpiperazin-1-yl)pyridine-3,4-diamine (LXXXIII) as purple solid (330 mg, 1.59 mmol, 99% yield). ^1H NMR (DMSO-d6, 500 MHz,): δ 2.18 (s, 3H), 2.34-2.36 (m, 4H), 3.13-3.16 (m, 4H), 3.89 (s, 2H), 5.20 (s, 2H), 5.94 (s, 1H), 7.31 (s, 1H); ESIMS found $C_{10}H_{17}N_5$ m/z 208 (M+H).

The following compound was prepared in accordance with the procedure described in the above Scheme 15.

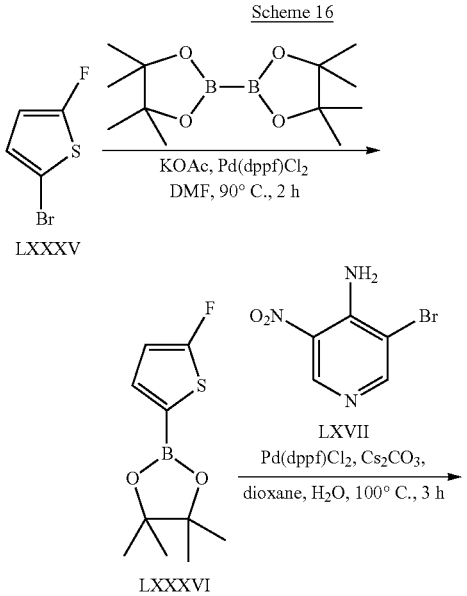
LXXXIV



5-(Piperidin-1-yl)pyridine-3,4-diamine (LXXXIV): Purple solid, (83% yield). ESIMS found $C_{10}H_{16}N_4$ m/z 193.1 (M+H).

Preparation of intermediate 5-(5-fluorothiophen-2-yl) pyridine-3,4-diamine (LXXXVIII) is depicted below in Scheme 16.

Scheme 16



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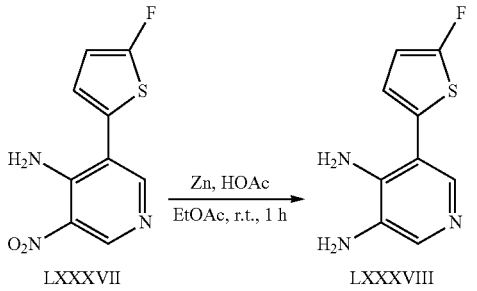


Step 1

A solution of 2-bromo-5-fluorothiophene (LXXXV) (3 g, 16.57 mmol, 1.0 eq) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (6.31 g, 24.86 mmol, 1.50 eq), $Pd(dppf)Cl_2$ (1.21 g, 1.66 mmol, 0.10 eq) and KOAc (4.07 g, 41.43 mmol, 2.5 eq) in dioxane (100 mL) was de-gassed and then heated to 90° C. for 8 h under N_2. TLC (EtOAc) showed the starting material was consumed completely. The reaction mixture was poured into H_2O (10 mL). The mixture was extracted with EtOAc (3×50 mL). The organic phase was washed with saturated brine (20 mL), dried over anhydrous $MgSO_4$, concentrated in vacuum to give 2-(5-fluorothiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (LXXXVI), which was used directly for next step without further purification.

Step 2

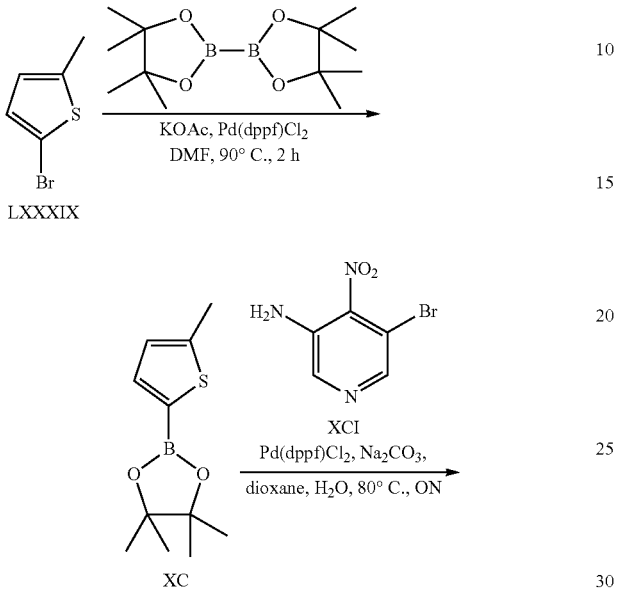
A solution of 3-bromo-5-nitropyridin-4-amine (LXVII) (800 mg, 3.67 mmol), 2-(5-fluorothiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (LXXXVI) (1.0 g, 4.4 mmol, 1.2 eq), $Pd(dppf)Cl_2$ (268 mg, 0.37 mmol, 0.1 eq) and Cs_2CO_3 (2.39 g, 7.34 mmol, 2.0 eq) in dioxane (20 mL) and H_2O (4 mL) was de-gassed and then heated to 100° C. under N_2 for 3 h. TLC (PE:EtOAc=1:1) showed the starting material was consumed completely. The mixture was concentrated in vacuum to give a residue, which was purified by column chromatography (PE:EtOAc=1:1) to afford the 3-(5-fluorothiophen-2-yl)-5-nitropyridin-4-amine (LXXXVII) (540 mg, 2.26 mmol, 61.5% yield). ESIMS found $C_9H_6FN_3O_2S$ m/z 240.1 (M+H).

Step 3

To a solution of 3-(5-fluorothiophen-2-yl)-5-nitropyridin-4-amine (LXXXVII) (500 mg, 2.09 mmol, 1 eq) in EtOAc (20 mL) was added Zn power (410 mg, 6.27 mmol, 3 eq), then cooled to 0~5° C. HOAc (3 mL) was then added dropwise, the mixture was stirred at 15~20° C. for 1 h. LC/MS showed the starting material was consumed completely. The mixture was filtered through Celite®, washed with EtOAc (5×50 mL), the organic phase was washed with $NaHCO_3$ (50 mL×2), brine (50 mL), water, then concentrated to dryness to afford 5-(5-fluorothiophen-2-yl)pyridine-3,4-diamine (LXXXVIII) (400 mg, 1.91 mmol, 91.5% yield). ESIMS found $C_9H_8FN_3S$ m/z 210.0 (M+H).

Preparation of intermediate 5-(5-methylthiophen-2-yl) pyridine-3,4-diamine (XCIII) is depicted below in Scheme 17.

Scheme 17



Step 1

4,4,5,5-Tetramethyl-2-(5-methylthiophen-2-yl)-1,3,2-dioxaborolane (XC) was prepared following the procedure in Scheme 16, step 1 above. Product was used directly for next step without further purification.

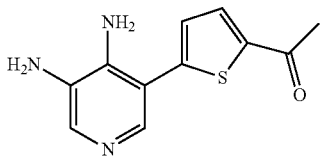
Step 2

A solution of 4,4,5,5-Tetramethyl-2-(5-methylthiophen-2-yl)-1,3,2-dioxaborolane (XC) (2.23 g, 9.95 mmol, 1.2 eq), 5-bromo-4-nitropyridin-3-amine (XCI) (1.80 g, 8.26 mmol, 1.0 eq), Na_2CO_3 (3.08 g, 29.01 mmol, 3.5 eq) and Pd(dppf) Cl_2 (307.47 mg, 414.50 μmol, 0.05 eq) in dioxane (40 mL) and H_2O (8 mL) was de-gassed and then heated to 80° C. overnight under N_2. TLC (PE:EtOAc=1:1) showed the starting material was consumed completely. The reaction mixture was poured into H_2O (300 mL). The mixture was extracted with EtOAc (3×250 mL). The organic phase was washed with saturated brine (300 mL), dried over anhydrous $NaSO_4$, concentrated in vacuum to give a residue. The crude product was purified by silica gel chromatography (PE: EtOAc=10:1) to give 5-(5-methylthiophen-2-yl)-4-nitropyridin-3-amine (XCII) (1.20 g, 5.10 mmol, 61.8% yield) as brown solid. ESIMS found $C_{10}H_9N_3O_2S$ m/z 236.1 (M+H).

Step 3

To a mixture of 5-(5-methylthiophen-2-yl)-4-nitropyridin-3-amine (XCII) (1.20 g, 5.10 mmol, 1.0 eq) in MeOH (30 mL) and H_2O (10 mL), was added Fe (1.14 g, 20.48 mmol, 4.0 eq) and NH_4Cl (2.20 g, 40.96 mmol, 8.0 eq) in one portion at room temperature. The mixture was stirred at room temperature for 10 min. Then heated to 80° C. and stirred for 16 hours. TLC showed the reaction was completed. The mixture was cooled to room temperature and concentrated in reduced pressure at 60° C. After filtration, the aqueous phase was extracted with EtOAc (400 mL×3). The combined organic phase was washed with saturated brine (200 mL×2), dried with anhydrous Na_2SO_4, filtered and concentrated in vacuum to produce 5-(5-methylthiophen-2-yl)pyridine-3,4-diamine (XCIII) (1.00 g, 4.87 mmol, 95.5% yield) as a brown oil. ^1H NMR (CD_3OD, 400 MHz) δ ppm 2.53 (s, 3H), 6.85 (d, J=3.2 Hz, 1H), 6.99 (d, J=3.6 Hz, 1H), 7.67 (s, 1H), 7.73 (s, 1H); ESIMS found $C_{10}H_{11}N_3S$ m/z 206.1 (M+H).

The following compound was prepared in accordance with the procedure described in the above Scheme 17.

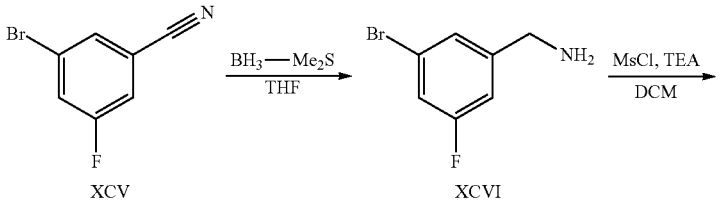


XCIV

1-(5-(4,5-Diaminopyridin-3-yl)thiophen-2-yl)ethan-1-one (XCIV): (2.3 g, 9.86 mmol, 56% yield). ^1H NMR (DMSO-d_6, 400 MHz) δ ppm 2.58 (s, 3H), 4.87 (brs, 2H), 5.46 (brs, 2H), 7.35 (s, 1H), 7.57-7.80 (m, 2H), 8.00 (s, 1H); ESIMS found $C_{11}H_{11}N_3OS$ m/z 234.0 (M+H).

Preparation of intermediate N-(3-(4,5-diaminopyridin-3-yl)-5-fluorobenzyl)methanesulfonamide (C) is depicted below in Scheme 18.

Scheme 18



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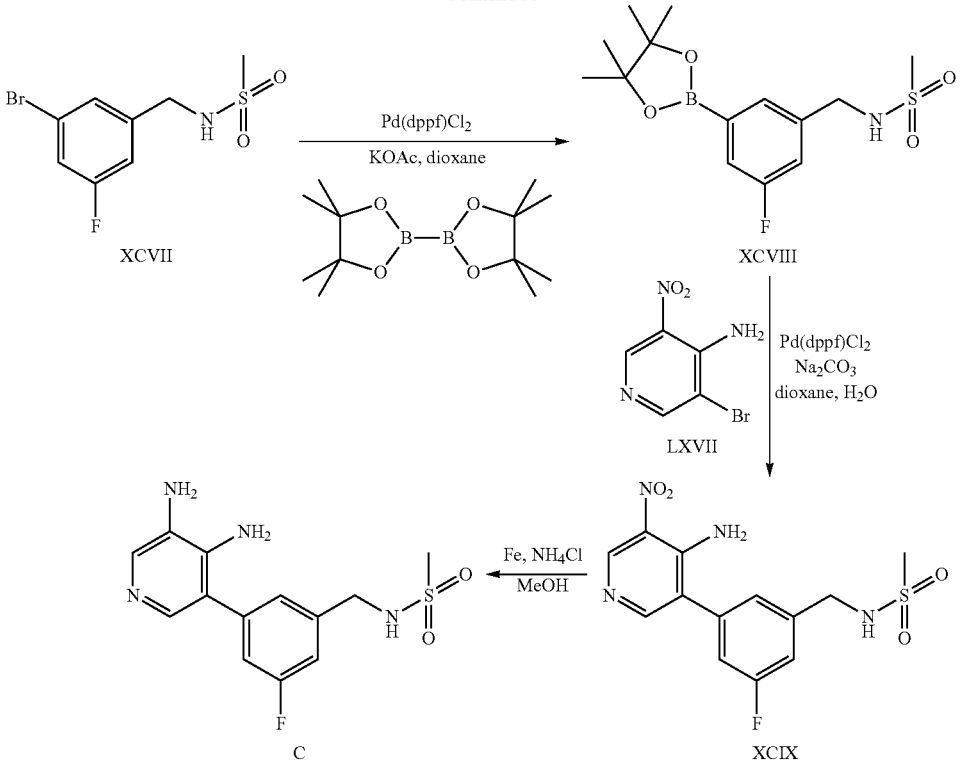


Step 1

A solution of 3-bromo-5-fluorobenzonitrile (XCV) (44.0 g, 220.0 mmol, 1.0 eq) was dissolved in THF (30 mL). BH_3-Me_2S (33.43 g, 440.0 mmol, 2.0 eq) was added to the solution at 20° C. Then it was stirred at 80° C. for 2 h, HCl (6 N, 100 mL) was added to the mixture slowly at 20° C. The mixture was stirred at 80° C. for 1 h, then it was washed with EtOAc (300 ml). The water phase was basified with 50% aqueous NaOH and it was extracted with EtOAc (300 mL×3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo to produce (3-bromo-5-fluoro-phenyl)methanamine (XCVI) (24.0 g, 117.62 mmol, 53.5% yield). ^1H NMR ($CDCl_3$, 300 MHz) 3.86 (s, 2H), 7.01 (d, J=8 Hz, 1H), 7.12 (d, J=8 Hz, 1H), 7.28 (s, 1H); ESIMS found C_7H_7BrFN m/z 203.9 ($Br^{79}M+H$).

Step 2

A solution of (3-bromo-5-fluoro-phenyl)methanamine (XCVI) (23.0 g, 112.7 mmol, 1.0 eq) was dissolved in DCM (15 mL), TEA (34.22 g, 338.2 mmol, 3.0 eq) was added to the mixture. Then MsC1 (13.44 g, 117.3 mmol, 1.04 eq) was added slowly to the solution at 0° C. It was stirred at 0-30° C. for 2 h. The reaction was washed with water and extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated to give N-(3-bromo-5-fluorobenzyl) methanesulfonamide (XCVII) (34.0 g, 102.44 mmol, 90.9% yield, 85% purity) as an oil. ^1H NMR ($CDCl_3$, 300 MHz) 2.88 (s, 3H), 4.24 (d, J=4.5 Hz, 2H), 6.99 (d, J=9 Hz, 1H), 7.13 (dt, J=8.1 Hz, J=2 Hz, 1H), 7.25 (s, 1H); ESIMS found $C_8H_9BrFNO_2S$ m/z 282.0 ($Br^{79}M+H$).

Step 3

A solution of N-(3-bromo-5-fluorobenzyl)methanesulfonamide (XCVII) (34.0 g, 102.4 mmol, 1.0 eq) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (52.02 g, 204.9 mmol, 2.0 eq), KOAc (20.11 g, 204.9 mmol, 2.0 eq) was dissolved in dioxane (20 mL). Then $Pd(dppf)Cl_2$ (7.60 g, 10.2 mmol, 0.1 eq) was added to the mixture. It was stirred at 90° C. for 2 h. Then the solvent was removed to get the residue which was purified by silica gel column (PE:EtOAc=10:1→100% EtOAc) to get N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)methanesulfonamide (XCVIII) (30.0 g, crude). ^1H NMR ($CDCl_3$, 400 MHz) 1.37 (s, 12H), 2.92 (s, 3H), 4.34 (d, J=6.3 Hz, 2H), 7.19 (dt, J=9.3 Hz, J=2.1 Hz, 1H), 7.44 (dd, J=8.7 Hz, J=2.4 Hz, 1H), 7.54 (s, 1H); ESIMS found $C_{14}H_{21}BFNO_4S$ m/z 330.1 (M+H).

Step 4

A solution of N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)methanesulfonamide (XCVIII) (3.26 g, 9.90 mmol, 1.2 eq), 3-bromo-5-nitropyridin-4-amine (LXVII) (1.80 g, 8.29 mmol, 1 eq), Na_2CO_3 (3.08 g, 29.01 mmol, 3.5 eq) and $Pd(dppf)Cl_2$ (307.47 mg, 414.50 μmol, 0.05 eq) in dioxane (20 mL) and H_2O (5 mL) was de-gassed and then heated to 80° C. overnight under N_2. TLC (PE:EtOAc=1:1) showed the starting material was consumed completely. The reaction mixture was poured into H_2O (300 mL). The mixture was extracted with EtOAc (3×250 mL). The organic phase was washed with saturated brine (300 mL), dried over anhydrous $NaSO_4$, concentrated in vacuum to give a residue. The crude product was purified by silica gel chromatography (PE:EtOAc=10:1) to give N-(3-(4-amino-5-nitropyridin-3-yl)-5-fluorobenzyl) methanesulfonamide (XCIX) (1.70 g, 5.0 mmol, 60.3% yield) as brown solid. ESIMS found for $C_{13}H_{13}FN_4O_4S$ m/z 341.1 (M+H).

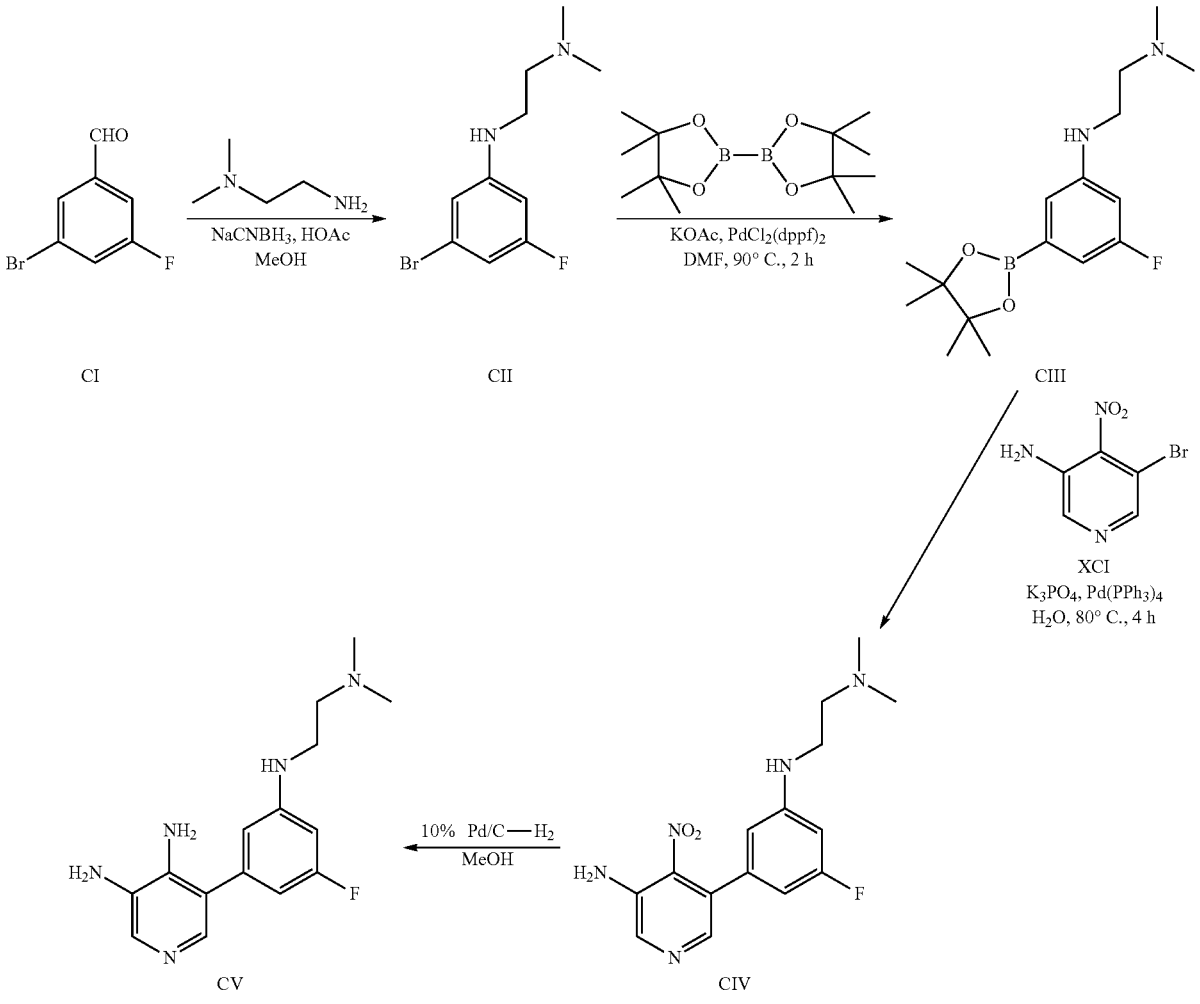
Step 5

To a solution of N-(3-(4-amino-5-nitropyridin-3-yl)-5-fluorobenzyl) methanesulfonamide (XCIX) (1.70 g, 5.0 mmol, 1 eq) in MeOH (30 mL), was added Fe (1.12 g, 20.0

mmol, 4.0 eq) and NH_4Cl (2.14 g, 40.0 mmol, 8 eq) in one portion at room temperature. The mixture was stirred at room temperature for 10 min. Then heated to 80° C. and stirred for 16 hours. TLC showed the reaction was completed. The mixture was cooled to room temperature and concentrated in reduced pressure at 60° C. The combined organic phase was washed with saturated brine (100 mL×2), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to yield N-(3-(4,5-diaminopyridin-3-yl)-5-fluorobenzyl) methanesulfonamide (C) (1.20 g, 3.87 mmol, 77.3% yield) as a brown solid. ^1H NMR (DMSO-d_6, 400 MHz) δ ppm 2.93 (s, 3H), 4.24 (d, J=6.4 Hz, 2H), 4.80 (brs, 2H), 5.12 (brs, 2H), 7.15 (dd, J=9.6 Hz, J=19.6 Hz, 2H), 7.23 (s, 1H), 7.47 (s, 1H), 7.66 (t, J=6.8 Hz, 1H), 7.68 (s, 1H); ESIMS found for $C_{13}H_{15}FN_4O_2S$ m/z 311.1 (M+H).

Preparation of intermediate 5-(3-((2-(dimethylamino) ethyl)amino)-5-fluorophenyl)pyridine-3,4-diamine (CV) is depicted below in Scheme 19.

Scheme 19



Step 1

A solution of 3-bromo-5-fluorobenzaldehyde (CI) (20.0 g, 98.2 mmol, 1.0 eq) in MeOH (1.8 L) was added N^1,N^1-dimethylethane-1,2-diamine (21.5 mL, 196.4 mmol, 2.0 eq). The pH was adjusted to 6 using HOAc and stirred for 1 h. $NaCNBH_3$ (8.6 g, 137.5 mmol, 1.4 eq) was added and stirred at room temperature overnight. The MeOH was removed under vacuum and the residue was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated under vacuum. The crude product was purified on a silica gel column (100% $CHCl_3$→3:97 MeOH[7N NH_3]:$CHCl_3$) to produce N^1-(3-bromo-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CII) as a yellow oil (13.0 g, 49.9 mmol, 51% yield). ^1H NMR (DMSO-d_6, 500 MHz) δ ppm 1.28 (s, 6H), 2.39 (t, J=4 Hz, 2H), 3.07 (q, J=6 Hz, 2H), 6.10 (t, J=5 Hz, 1H), 6.38 (td, J=12 Hz, J=2 Hz, 1H), 6.51 (td, J=8.6 Hz, J=2 Hz, 1H), 6.61 (t, J=2 Hz, 1H); ESIMS found $C_{10}H_{14}BrFN_2$ m/z 261.0 (M+H).

Step 2

A solution of N^1-(3-bromo-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CII) (13.0 g, 49.9 mmol, 1.0 eq), bis(pinacolato)diboron (12.6 g, 59.9 mmol, 1.2 eq), KOAc (12.1 g, 124.3 mmol, 2.5 eq) and dioxane (600 mL) was purged with argon. $Pd(dppf)Cl_2$ (2.0 g, 2.47 mmol, 0.05 eq) was added to the reaction and purged again with argon. The solution was heated at 90° C. for 2 h. Once TLC showed the disappearance of (CII), the solution was cooled to room temperature and then concentrated under reduced pressure to produce crude N^1-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-di-

oxaborolan-2-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine (CIII) (7.4 g, 24.0 mmol, 48.2% yield).

Step 3

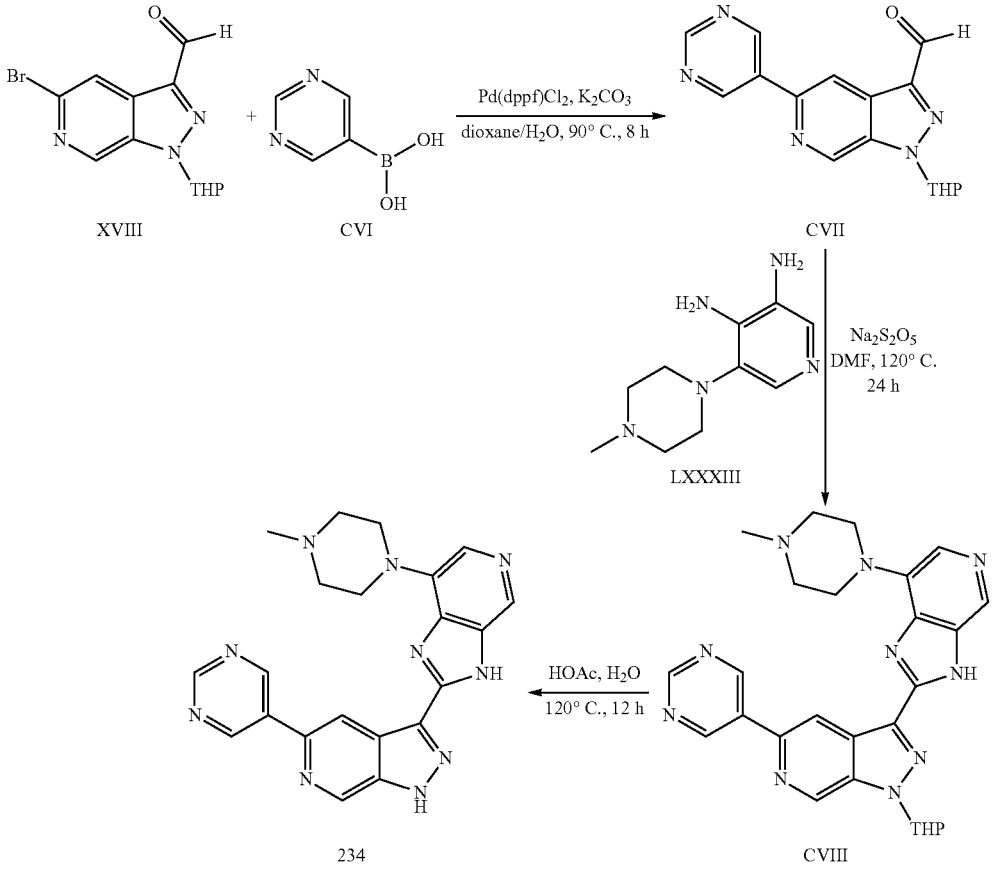
To a solution of N^1-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine (CIII) (5.0 g, 16.22 mmol, 1.0 eq), 5-bromo-4-nitropyridin-3-amine (XCI) (3.53 g, 16.22 mmol, 1.0 eq) in dioxane (100 mL) and H_2O (25 mL) was added $Pd(dppf)Cl_2$ (593 mg, 811 μmol, 0.05 eq) and K_2CO_3 (3.18 g, 32.44 mmol, 2 eq), the resulting solution was heated to 100° C. for 48 hr under N_2. The mixture was concentrated in vacuum to give a residue, which was pre-purified by column chromatography to afford N^1-(3-(5-amino-4-nitropyridin-3-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CIV) (4.5 g, 14.09 mmol, 86.9% yield). ESIMS found for $C_{15}H_{18}FN_5O_2$ m/z 320.1 (M+H).

Step 4

To a solution of N^1-(3-(5-amino-4-nitropyridin-3-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CIV) (4.50 g, 14.09 mmol, 1.0 eq) in MeOH (15 mL) was added Pd—C under N_2. The suspension was degassed under vacuum and purged with H_2 several times. The mixture was stirred under H_2 (15psi) at room temperature for 48 hours. TLC showed the starting material was consumed completely. The reaction mixture was filtered and the filter was concentrated. The crude product was purified by silica gel chromatography (MeOH:DCM=10:1) to give 5-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)pyridine-3,4-diamine (CV) (750.0 mg, 2.59 mmol, 18.4% yield). ^1H NMR (CD_3OD, 400 MHz) δ ppm 2.32 (s, 6H), 2.60 (t, J=6.8 Hz, 2H), 3.26 (t, J=6.8 Hz, 2H), 6.33-6.43 (m, 2H), 6.47 (d, J=1.6 Hz, 1H), 7.58 (s, 1H), 7.75 (s, 1H); ESIMS found $C_{15}H_{20}FN_5$ m/z 290.1 (M+H).

Preparation of 3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine (234) is depicted below in Scheme 20.

Scheme 20



Step 1

To a solution of 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-c]pyridine-3-carbaldehyde (XVIII) (3.0 g, 9.67 mmol, 1.0 eq) and pyrimidin-5-ylboronic acid (CVI) (1.80 g, 14.51 mmol, 1.5 eq) in dioxane (60 mL) and H_2O (5 mL) was added $Pd(dppf)Cl_2$ (354 mg, 483.6 μmol, 0.05 eq), K_2CO_3 (3.34 g, 24.2 mmol, 2.5 eq) at room temperature. The mixture was stirred at 90° C. for 3 hr. TLC (PE:EtOAc=0:1) showed that the starting material was consumed completely. The mixture was added water (50 mL) and extracted with EtOAc (50 mL×3). The organic layers were washed with brine (50 mL×2), concentrated. The residue was purified by chromatography on silica gel (PE:EtOAc=1:1→1:5) to afford 5-(pyrimidin-5-yl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-c]pyridine-3-carbaldehyde (CVII) (2.0 g, 6.47 mmol, 66.9% yield) as a red brown solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.59-1.93 (m, 3H), 2.09-2.22 (m, 1H), 2.22-2.31 (m, 1H), 2.47-2.62 (m, 1H), 3.80-3.92 (m, 1H), 3.97-4.10 (m, 1H), 6.00 (dd, J=3.2 Hz, J=8.4 Hz, 1H), 8.64 (s, 1H), 9.28 (s, 1H), 9.39 (d, J=2.4 Hz, 1H), 9.44 (s, 2H), 10.31 (s, 1H); ESIMS found for $C_{16}H_{15}N_5O_2$ m/z 310.1 (M+H).

Step 2

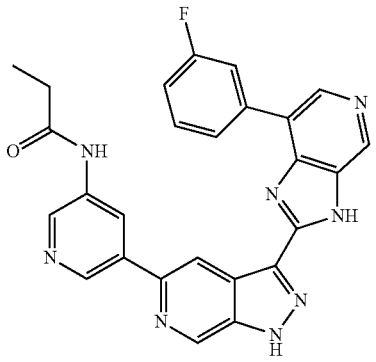
A mixture of 5-(pyrimidin-5-yl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-c]pyridine-3-carbaldehyde (CVII) (100.0 mg, 0.32 mmol, 1 eq), 5-(4-methylpiperazin-1-yl) pyridine-3,4-diamine (LXXXIII) (67 mg, 0.32 mmol, 1.0 eq) and $Na_2S_2O_5$ (74 mg, 0.39 mmol, 1.2 eq) in DMF (2 mL) was stirred at 120° C. for 24 h. LC/MS showed the starting material was consumed. Water (5 mL) was added in dropwise and the mixture was filtered. The filtrate was washed by MeOH (0.5 mL) and used for directly for next step without further purification.

Step 3

A solution of 3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-c]pyridine (CVIII) in HOAc/H_2O (15 mL) was stirred at 120° C. for 12 h. LC/MS showed the starting material was consumed. The mixture was concentrated to give a residue and purified by pre-HPLC (HCl) to give 3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine (234) (12.0 mg, 0.03 mmol, 9.0% yield for 2 steps) as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.84 (d, J=4.14 Hz, 3H), 3.15-3.31 (m, 2H), 3.44-3.64 (m, 2H), 4.32 (d, J=12.92 Hz, 4H), 7.19 (brs, 1H), 8.82 (s, 1H), 8.90 (s, 1H), 9.26 (s, 1H), 9.38 (d, J=1.13 Hz, 1H), 9.49 (s, 2H), 11.29 (brs, 1H), 14.96 (brs, 1H); ESIMS found for $C_{21}H_{20}N_{10}$ m/z 413.1 (M+1).

The following compound was prepared in accordance with the procedure described in the above Example 1.

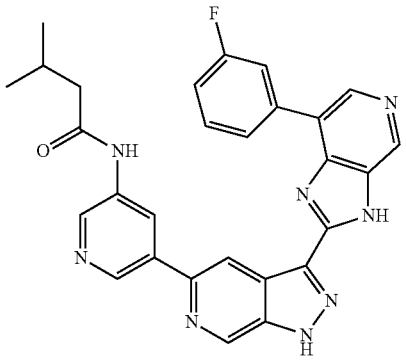
1



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide 1.

White solid (19.2 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.14 (t, J=7.53 Hz, 3H), 2.43 (q, J=7.53 Hz, 2H), 7.31 (td, J=8.50, 2.57 Hz, 1H), 7.62-7.72 (m, 1H), 8.27 (s, 1H), 8.41 (s, 1H), 8.80 (brs, 2H), 8.85-8.97 (m, 3H), 8.98 (d, J=1.88 Hz, 1H), 9.35 (s, 1H), 10.32 (s, 1H); ESIMS found for $C_{26}H_{19}FN_8O$ m/z 479.1 (M+1).

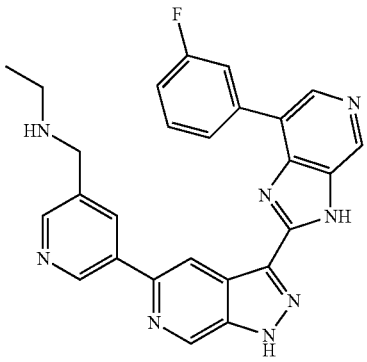
2



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 2.

Light brown solid (2.3 mg, 0.005 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.99 (d, J=6.5 Hz, 6H), 2.14 (non, J=6.5 Hz, 1H), 2.29 (d, J=7.5 Hz, 2H), 7.30 (td, J=2.5 Hz, J=8.5 Hz, 1H), 7.66 (q, J=8 Hz, 1H), 8.26 (brs, 1H), 8.40 (brs, 1H), 8.76 (brs, 1H), 8.80 (s, 1H), 8.89 (s, 1H), 8.92 (brs, 1H), 8.95 (s, 1H), 8.98 (d, J=1.5 Hz, 1H), 9.35 (d, J=1 Hz, 1H), 10.23 (s, 1H), 13.93 (brs, 1H), 14.48 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 506.9 (M+1).

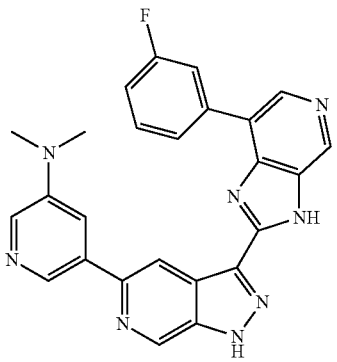
6



N-((5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine 6.

White solid (74.6 mg, 0.16 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.30 (t, J=7.22 Hz, 3H), 3.01-3.14 (m, 2H), 4.40 (t, J=5.14 Hz, 2H), 7.45 (td, J=8.60, 2.26 Hz, 1H), 7.75 (q, J=6.8 Hz, 1H), 8.09-8.38 (m, 2H), 8.95 (brs, 1H), 8.97-9.02 (m, 2H), 9.06 (brs, 1H), 9.23 (brs, 1H), 9.38 (s, 1H), 9.42 (d, J=1.38 Hz, 1H), 9.70 (brs, 2H), 15.25 (brs, 1H); ESIMS found for $C_{26}H_{21}FN_8$ m/z 465.1 (M+1).

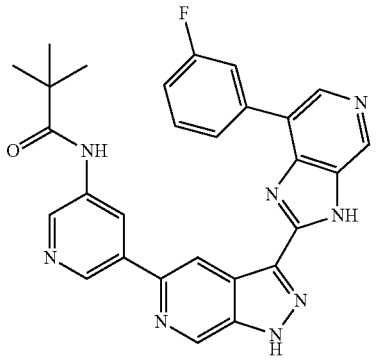
7



5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine 7.

White solid (46.2 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.18 (s, 6H), 7.43 (td, J=9.04 Hz, J=1.40 Hz, 1H), 7.75 (q, J=7.57 Hz, 1H), 8.28 (s, 3H), 8.71 (s, 1H), 8.94 (brs, 1H), 9.02 (s, 1H), 9.26 (brs, 1H), 9.42 (s, 1H), 15.17 (brs, 1H); ESIMS found for $C_{25}H_{19}FN_8$ m/z 451.1 (M+1).

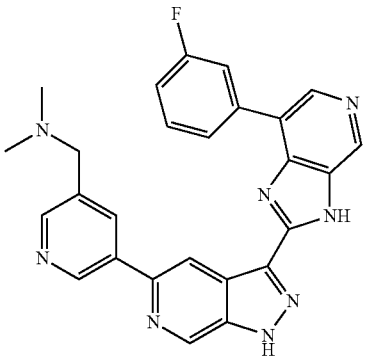
8



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide 8.

White solid (25.2 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.30 (s, 9H), 7.29 (td, J=8.38, 2.20 Hz, 1H), 7.66 (q, J=6.76 Hz, 1H), 8.16 (s, 1H), 8.24 (brs, 1H), 8.41 (brs, 1H), 8.75 (brs, 1H), 8.85 (s, 1H), 8.94 (d, J=2.38 Hz, 3H), 9.01 (d, J=1.76 Hz, 1H), 9.35 (s, 1H), 9.61 (s, 1H), 13.99 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ nm/z 507.1 (M+1).

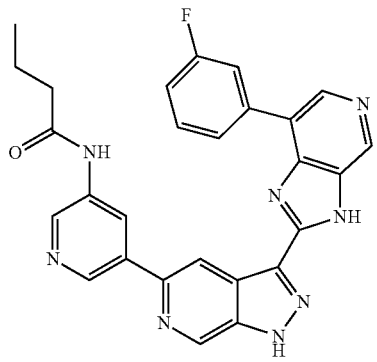
13



1-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 13.

White solid (29.3 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.38 (brs, 6H), 3.80 (brs, 2H), 7.34 (t, J=8.72 Hz, 1H), 7.59-7.73 (m, 1H), 8.19-8.28 (m, 1H), 8.46 (d, J=5.40 Hz, 2H), 8.59 (brs, 1H), 8.77 (brs, 1H), 8.89 (brs, 1H), 8.98 (brs, 1H), 9.29 (brs, 1H), 9.34 (brs, 1H), 13.93 (brs, 1H), 14.58 (s, 1H); ESIMS found for $C_{26}H_{21}FN_8$ m/z 465.1 (M+1).

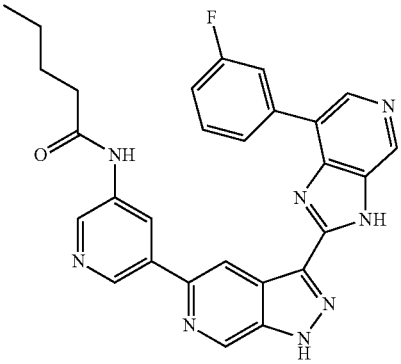
17



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 17.

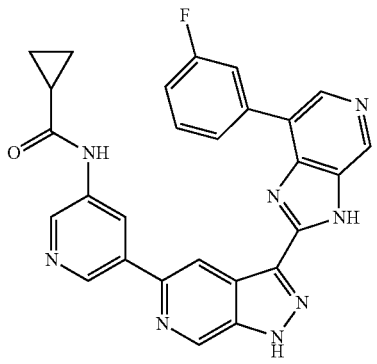
White solid (17.8 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.97 (t, J=7.34 Hz, 3H), 1.68 (sxt, J=7.33 Hz, 2H), 2.43 (t, J=7.34 Hz, 2H), 7.39 (t, J=8.60 Hz, 1H), 7.73 (q, J=7.52 Hz, 1H), 8.24 (brs, 2H), 8.85 (brs, 1H), 8.93 (brs, 2H), 9.01 (brs, 2H), 9.21 (brs, 1H), 9.34 (brs, 1H), 10.69 (brs, 1H), 15.09 (brs, 1H); ESIMS found for $C_{27}H_{21}FN_8O$ m/z 493.1 (M+1).

18



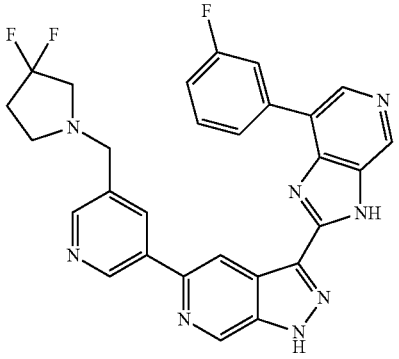
N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 18.

White solid (71.4 mg, 0.14 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.28 Hz, 3H), 1.37 (sxt, J=7.52 Hz, 2H), 1.63 (quin, J=7.40 Hz, 2H), 2.41 (t, J=7.40 Hz, 2H), 7.34 (td, J=8.44, 2.32 Hz, 1H), 7.67 (q, J=6.4 Hz, 1H), 8.18 (brs, 1H), 8.28 (brs, 1H), 8.77 (d, J=2.01 Hz, 1H), 8.81 (s, 1H), 8.87 (s, 2H), 8.95 (d, J=1.51 Hz, 1H), 9.05 (brs, 1H), 9.34 (s, 1H), 10.27 (s, 1H), 14.68 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.2 (M+1).



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide 19.

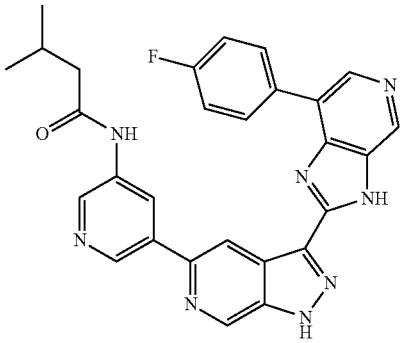
White solid (36.8 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.87-1.00 (m, 4H), 1.93-2.03 (m, 1H), 7.40 (td, J=8.47, 1.88 Hz, 1H), 7.72-7.83 (m, 1H), 8.21 (brs, 2H), 8.90 (s, 1H), 8.95 (brs, 1H), 9.12 (d, J=4.64 Hz, 2H), 9.23 (s, 2H), 9.36 (s, 1H), 11.51 (brs, 1H), 15.21 (brs, 1H); ESIMS found for $C_{27}H_{19}FN_8O$ m/z 491.1 (M+1).



5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 25.

White solid (69.8 mg, 0.13 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.57-2.69 (m, 2H), 3.82-3.95 (m, 4H), 4.63 (brs, 2H), 7.46 (td, J=8.69, 2.07 Hz, 1H), 7.75 (q, J=6.68 Hz, 1H), 8.28 (brs, 2H), 8.93-9.06 (m, 4H), 9.22-9.33 (m, 1H), 9.41 (s, 1H), 9.43 (s, 1H), 15.21 (brs, 1H); ESIMS found for $C_{28}H_{21}F_3N_8$ m/z 527.1 (M+1).

28

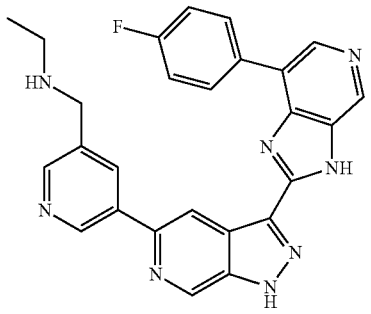


19

N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 28.

White solid (11.6 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.99 (d, J=6.53 Hz, 6H), 2.16 (non, J=6.92 Hz, 2H), 2.36 (d, J=7.15 Hz, 2H), 7.53 (t, J=8.85 Hz, 2H), 7.68 (q, J=5.88 Hz, 1H), 8.78 (s, 1H), 8.90 (s, 1H), 9.10 (d, J=1.76 Hz, 2H), 9.15 (s, 1H), 9.29-9.65 (m, 2H), 9.41 (s, 1H), 11.02 (brs, 1H), 15.21 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.1 (M+1).

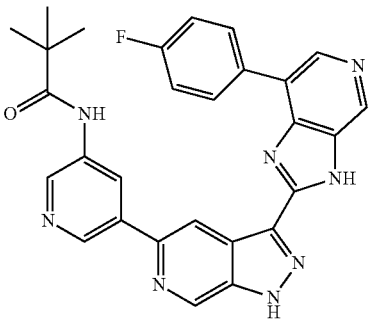
32



N-((5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine 32.

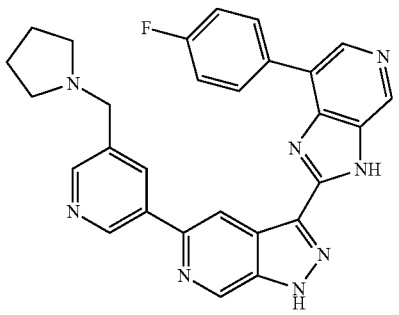
White solid (26.5 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.29 (t, J=7.22 Hz, 3H), 3.01-3.12 (m, 2H), 4.38 (t, J=5.65 Hz, 2H), 7.53 (t, J=8.4 Hz, 2H), 7.66-7.75 (m, 1H), 8.79 (s, 1H), 8.93 (s, 1H), 8.97 (brs, 1H), 8.99 (s, 1H), 9.35-9.65 (m, 2H), 9.40 (brs, 1H), 9.42 (d, J=1.13 Hz, 1H), 9.56 (brs, 2H), 15.18 (brs, 1H); ESIMS found for $C_{26}H_{21}FN_8$ m/z 465.1 (M+1).

34



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide 34.

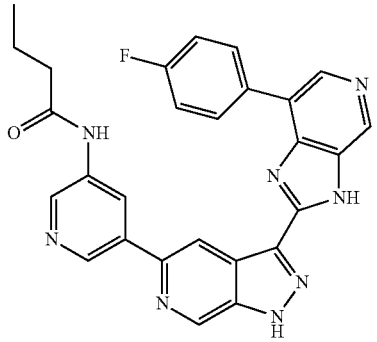
White solid (37.4 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.32 (s, 9H), 7.46-7.58 (m, 2H), 7.63-7.73 (m, 1H), 8.79 (brs, 1H), 8.89 (s, 1H), 9.10 (brs, 1H), 9.15 (brs, 2H), 9.42 (s, 1H), 10.05 (brs, 1H), 15.08 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.1 (M+1).



3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 40.

White solid (25.0 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.84-1.98 (m, 2H), 2.01-2.13 (m, 2H), 3.13-3.25 (m, 2H), 3.47 (d, J=3.64 Hz, 2H), 4.69 (d, J=5.02 Hz, 2H), 7.48-7.58 (m, 2H), 7.65-7.75 (m, 1H), 7.97 (brs, 1H), 8.78 (s, 1H), 9.07 (s, 1H), 9.14 (d, J=1.38 Hz, 1H), 9.30 (brs, 1H), 9.42 (d, J=1.13 Hz, 1H), 9.46 (brs, 1H), 9.49 (s, 1H), 11.76 (brs, 1H), 15.33 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8$ m/z 491.1 (M+1).

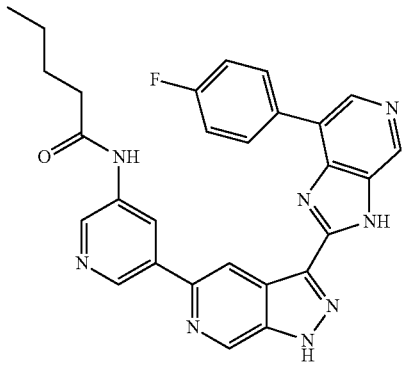
43



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 43.

White solid (25.0 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.97 (t, J=7.40 Hz, 3H), 1.69 (sxt, J=7.38 Hz, 2H), 2.46 (t, J=7.34 Hz, 3H), 7.53 (t, J=8.92 Hz, 2H), 7.63-7.72 (m, 1H), 7.95 (brs, 1H), 8.77 (s, 1H), 8.87 (s, 1H), 9.11 (brs, 2H), 9.17 (s, 1H), 9.38 (d, J=1.00 Hz, 1H), 9.45 (brs, 1H), 11.12 (brs, 1H), 15.21 (brs, 1H); ESIMS found for $C_{27}H_{21}FN_8O$ m/z 493.1 (M+1).

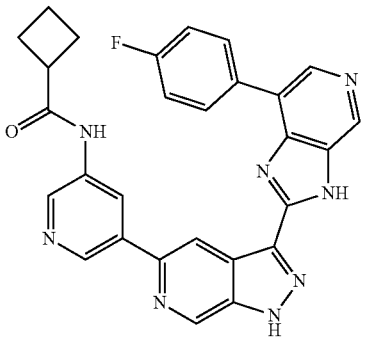
44



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 44.

White solid (57.9 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.34 Hz, 3H), 1.37 (sxt, J=7.43 Hz, 2H), 1.64 (quin, J=7.43 Hz, 2H), 2.41 (t, J=7.40 Hz, 2H), 7.44 (t, J=8.78 Hz, 2H), 7.52-7.61 (m, 1H), 7.95 (brs, 1H), 8.49 (brs, 1H), 8.82 (s, 3H), 8.94 (brs, 1H), 9.08 (brs, 1H), 9.32 (s, 1H), 10.28 (s, 1H), 14.56 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.1 (M+1).

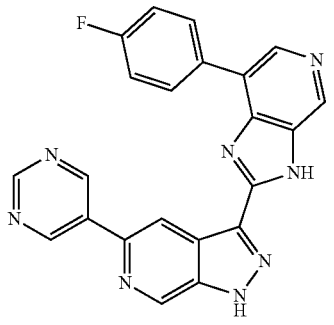
46



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide 46.

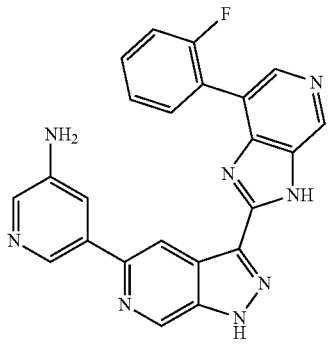
White solid (57.8 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.79-1.91 (m, 1H), 1.93-2.07 (m, 1H), 2.11-2.23 (m, 2H), 2.24-2.37 (m, 2H), 3.32 (quin, J=8.16 Hz, 1H), 7.44 (t, J=8.52 Hz, 2H), 7.561 (qd, J=7.52 Hz, J=1.64 Hz, 1H), 8.47 (brs, 1H), 8.83 (d, J=1.13 Hz, 3H), 8.95 (brs, 1H), 9.05 (brs, 1H), 9.33 (d, J=1.13 Hz, 1H), 10.14 (s, 1H), 14.55 (brs, 1H); ESIMS found for $C_{28}H_{21}FN_8O$ m/z 505.1 (M+1).

52



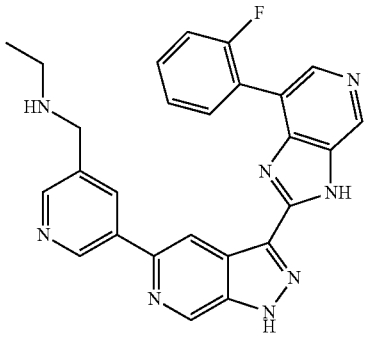
3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine 52.

White solid (11.7 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.46-7.56 (m, 2H), 7.66-7.75 (m, 1H), 7.92 (brs, 1H), 8.79 (s, 1H), 8.93 (d, J=0.75 Hz, 1H), 9.28 (s, 1H), 9.44 (d, J=1.26 Hz, 1H), 9.47 (s, 2H), 9.50 (brs, 1H), 15.05 (brs, 1H); ESIMS found for $C_{22}H_{13}FN_8$ m/z 409.2 (M+1).



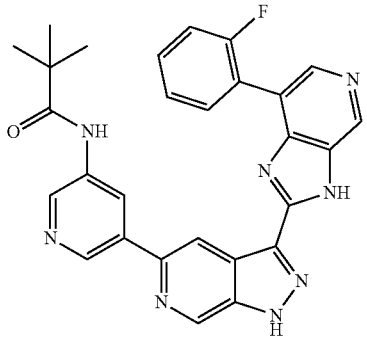
5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine 55.

White solid (19.9 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.58 (t, J=8.53 Hz, 2H), 8.12 (d, J=2.38 Hz, 1H), 8.40 (t, J=1.92 Hz, 2H), 8.43 (brs, 1H), 8.67 (s, 1H), 8.88 (brs, 1H), 8.89 (s, 1H), 9.23 (brs, 1H), 9.38 (d, J=1.13 Hz, 1H), 15.28 (brs, 1H); ESIMS found for $C_{23}H_{15}FN_8$ m/z 423.2 (M+1).



N-((5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine 58.

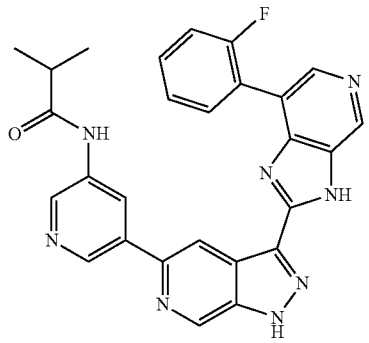
White solid (11.3 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.33 (t, J=7.22 Hz, 3H), 3.05-3.14 (m, 2H), 4.45 (brs, 2H), 7.54 (t, J=8.78 Hz, 2H), 8.37 (brs, 2H), 8.82 (s, 1H), 8.92 (s, 1H), 9.09 (s, 1H), 9.13 (brs, 1H), 9.21 (s, 1H), 9.32 (s, 1H), 9.43 (s, 1H), 9.89 (brs, 2H), 15.28 (brs, 1H); ESIMS found for $C_{26}H_{21}FN_8$ m/z 465.1 (M+1).



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide 60.

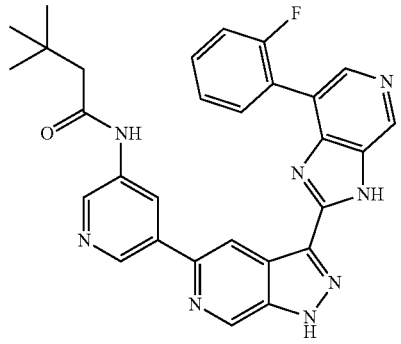
White solid (16.6 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.33 (s, 9H), 7.57 (t, J=8.53 Hz, 2H), 8.40-8.66 (m, 1H), 8.91 (d, J=1.00 Hz, 2H), 9.13-9.31 (m, 1H), 9.16 (d, J=1.63 Hz, 2H), 9.27 (brs, 1H), 9.42 (d, J=1.13 Hz, 1H), 10.16 (s, 1H), 15.16 (brs, 1H);

ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.1 (M+1).



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide 61.

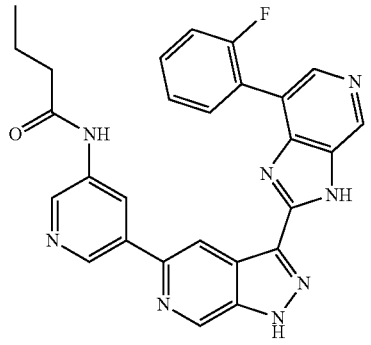
White solid (39.1 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.21 (d, J=6.90 Hz, 6H), 2.77 (spt, J=6.68 Hz, 1H), 7.59 (t, J=8.60 Hz, 2H), 8.51 (brs, 2H), 8.89 (s, 2H), 8.98 (brs, 1H), 9.13 (s, 1H), 9.20 (brs, 2H), 9.42 (d, J=0.88 Hz, 1H), 10.80 (brs, 1H), 15.13 (brs, 1H); ESIMS found for $C_{27}H_{21}FN_8O$ m/z 493.1 (M+1).



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide 68.

White solid (23.7 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.50 (s, 9H), 3.77 (s, 2H), 8.99 (t, J=8.41 Hz, 2H), 9.91 (brs, 2H), 10.32 (d, J=0.88 Hz, 2H), 10.41 (brs, 1H), 10.52-10.58 (m, 2H), 10.64 (brs, 1H), 10.84 (d, J=1.13 Hz, 1H), 12.17 (brs, 1H), 16.54 (brs, 1H); ESIMS found for $C_{29}H_{25}FN_8O$ m/z 521.2 (M+1).

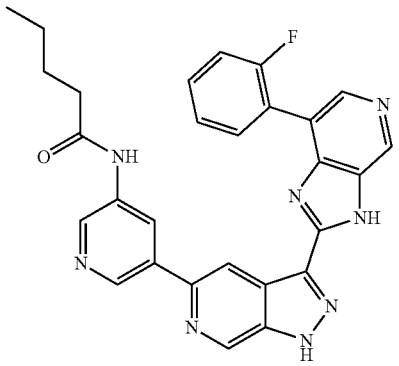
69



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 69.

White solid (16.7 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.97 (t, J=7.40 Hz, 3H), 1.69 (sxt, J=7.35 Hz, 2H), 2.47 (t, J=7.4 Hz, 2H), 7.51 (t, J=8.78 Hz, 2H), 8.36 (brs, 2H), 8.69 (brs, 1H), 8.80 (brs, 1H), 9.07 (brs, 3H), 9.19 (s, 1H), 9.23 (s, 1H), 11.25 (brs, 1H), 15.12-15.23 (m, 1H); ESIMS found for $C_{27}H_{21}FN_8O$ m/z 493.1 (M+1).

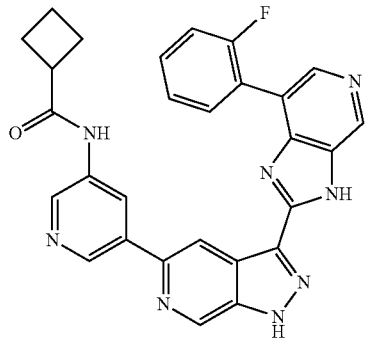
70



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 70.

White solid (79.6 mg, 0.16 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.40 Hz, 3H), 1.38 (sxt, J=7.40 Hz, 2H), 1.67 (quin, J=7.47 Hz, 2H), 2.43 (t, J=7.47 Hz, 2H), 7.47 (t, J=8.85 Hz, 2H), 8.40 (brs, 2H), 8.66 (brs, 1H), 8.71 (brs, 1H), 8.87 (s, 1H), 8.93 (brs, 2H), 9.00 (s, 1H), 9.33 (s, 1H), 10.31 (s, 1H), 14.57 (brs, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.1 (M+1).

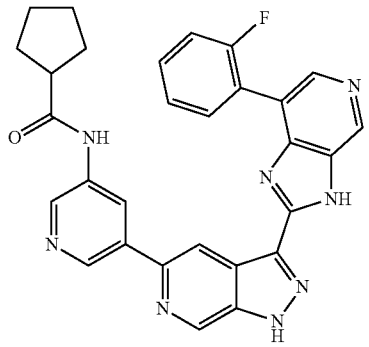
72



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide 72.

White solid (65.7 mg, 0.13 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.79-1.92 (m, 1H), 1.93-2.06 (m, 1H), 2.13-2.25 (m, 2H), 2.26-2.39 (m, 2H), 3.34 (quin, J=8.28 Hz, 2H), 7.50 (t, J=8.91 Hz, 2H), 8.39 (brs, 2H), 8.73 (s, 2H), 8.81 (d, J=1.00 Hz, 1H), 8.95 (s, 1H), 8.98 (d, J=1.76 Hz, 1H), 9.03 (brs, 1H), 9.33 (d, J=1.13 Hz, 1H), 10.16 (s, 1H), 14.68 (brs, 1H); ESIMS found for $C_{28}H_{21}FN_8O$ m/z 505.1 (M+1).

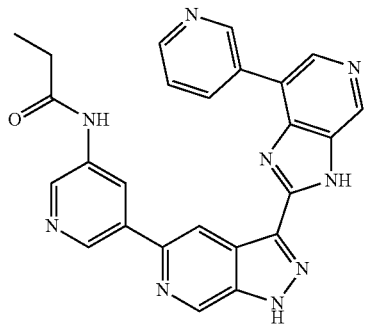
73



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide 73.

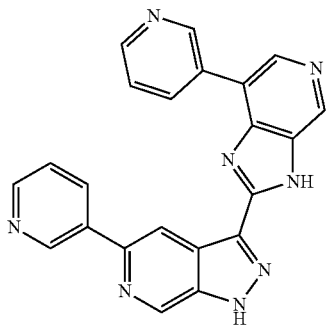
White solid (18.7 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.53-1.65 (m, 2H), 1.66-1.75 (m, 2H), 1.76-1.87 (m, 2H), 1.88-2.01 (m, 2H), 2.89 (quin, J=7.97 Hz, 1H), 7.48 (t, J=8.85 Hz, 2H), 8.40 (brs, 2H), 8.68 (brs, 1H), 8.74 (brs, 1H), 8.86 (s, 1H), 8.96 (brs, 2H), 9.00 (s, 1H), 9.34 (s, 1H), 10.32 (s, 1H), 14.63 (brs, 1H); ESIMS found for $C_{29}H_{23}FN_8O$ m/z 519.1 (M+1).

79



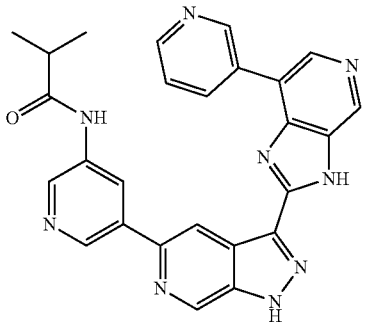
N-(5-(3-(7-(Pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide 79.

Brown solid (20 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.16 (t, J=7.5 Hz, 3H), 2.44 (q, J=7 Hz, 2H), 7.69 (s, 1H), 8.68 (s, 1H), 8.80 (s, 2H), 8.85 (d, 1H), 8.87-8.94 (m, 3H), 8.97 (s, 1H), 9.35 (s, 1H), 9.49 (s, 1H), 10.27 (s, 1H), 13.93 (brs, 1H), 14.58 (brs, 1H); ESIMS found for $C_{25}H_{19}N_9O$ m/z 462.0 (M+1).



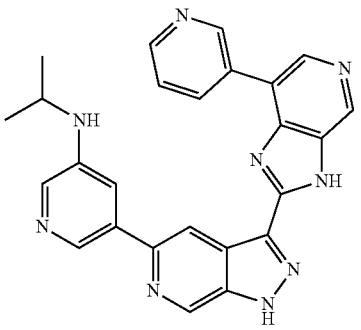
5-(Pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 82.

White solid (7.1 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.97-8.12 (m, 2H), 8.91 (d, J=4.52 Hz, 1H), 8.94 (d, J=4.89 Hz, 1H), 9.06 (brs, 3H), 9.35 (brs, 1H), 9.45 (s, 1H), 9.54 (s, 1H), 9.65 (brs, 1H), 15.22 (brs, 1H); ESIMS found for $C_{22}H_{14}N_8$ m/z 391.0 (M+1).



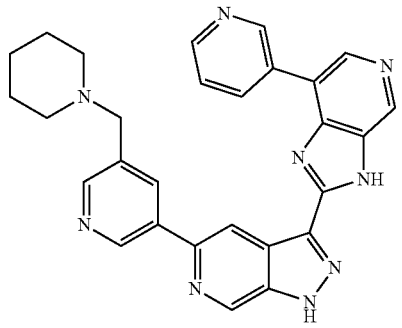
N-(5-(3-(7-(Pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide 87.

White solid (9.9 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.19 (d, J=6.78 Hz, 6H), 2.73 (spt, J=6.80 Hz, 1H), 7.91 (brs, 1H), 8.85 (d, J=4.77 Hz, 1H), 8.91 (s, 1H), 8.96 (s, 1H), 8.98-9.05 (m, 1H), 9.05-9.11 (m, 2H), 9.13 (brs, 1H), 9.32 (brs, 1H), 9.42 (s, 1H), 9.54 (brs, 1H), 10.58 (s, 1H), 15.05 (brs, 1H); ESIMS found for $C_{26}H_{21}N_9O$ m/z 476.1 (M+1).



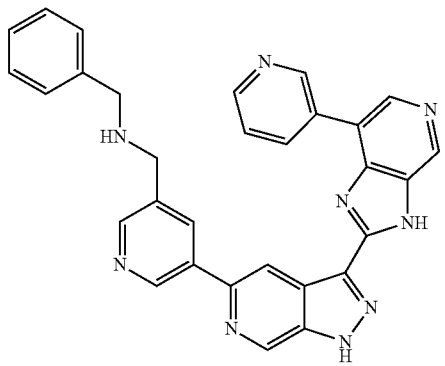
N-Isopropyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine 90.

White solid (64.2 mg, 0.14 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.21 (d, J=6.27 Hz, 6H), 3.72 (oct, J=7.16 Hz, 2H), 5.89 (d, J=8.16 Hz, 1H), 7.57 (t, J=2.13 Hz, 1H), 7.60 (dd, J=7.65, 4.89 Hz, 1H), 8.01 (d, J=2.64 Hz, 1H), 8.47 (d, J=1.88 Hz, 1H), 8.62-8.73 (m, 3H), 8.85 (d, J=1.13 Hz, 1H), 8.94 (s, 1H), 9.30 (d, J=1.13 Hz, 1H), 9.52 (brs, 1H); ESIMS found for $C_{25}H_{21}N_9$ m/z 448.1 (M+1).



5-(5-(Piperidin-1-ylmethyl)pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 93.

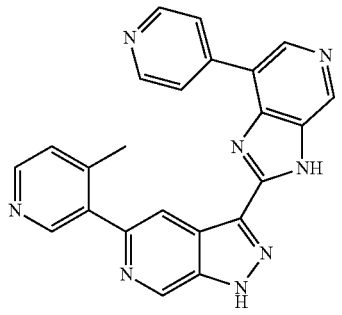
White solid (20.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.40 (brs, 1H), 1.66-1.76 (m, 1H), 1.82 (brs, 4H), 3.00 (brs, 2H), 3.40-3.49 (m, 2H), 4.63 (brs, 2H), 8.18 (d, J=6.52 Hz, 1H), 9.00-9.09 (m, 3H), 9.13 (brs, 1H), 9.22 (brs, 2H), 9.35 (brs, 1H), 9.42 (d, J=1.00 Hz, 1H), 9.53 (s, 1H), 9.81 (brs, 1H), 11.20 (brs, 1H), 15.30 (brs, 1H); ESIMS found for $C_{28}H_{25}N_9$ m/z 488.1 (M+1).



N-Benzyl-1-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine 101.

White solid (35.6 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 4.34 (brs, 2H), 4.59 (brs, 2H), 7.37-7.49 (m, 3H), 7.65 (d, J=6.27 Hz, 2H), 8.27 (brs, 1H), 8.99-9.10 (m, 3H), 9.16 (brs, 1H), 9.33 (brs, 2H), 9.42 (s, 1H), 9.55 (s, 1H), 9.85 (brs, 1H), 10.21 (d, J=4.52 Hz, 2H), 15.38 (brs, 1H); ESIMS found for $C_{30}H_{23}N_9$ m/z 510.1 (M+1).

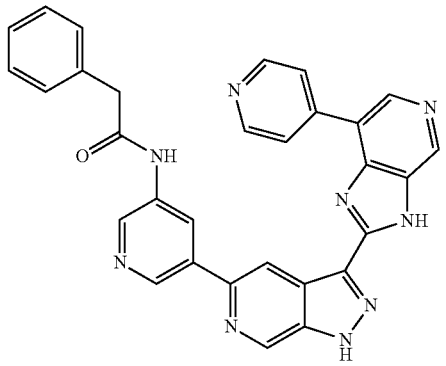
109



5-(4-Methylpyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 109.

White solid (11.3 mg, 0.03 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.82 (s, 3H), 8.17 (d, J=6.15 Hz, 1H), 8.84 (d, J=6.02 Hz, 1H), 8.89 (d, J=1.13 Hz, 1H), 9.10-9.16 (m, 3H), 9.16-9.21 (m, 2H), 9.26 (s, 1H), 9.43 (s, 1H), 9.45 (d, J=1.13 Hz, 1H); ESIMS found for $C_{23}H_{16}N_8$ m/z 405.0 (M+1).

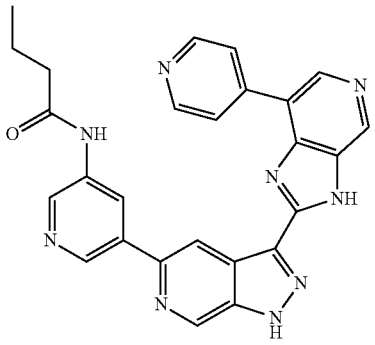
114



2-Phenyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide 114

White solid (33.9 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm 3.78 (s, 2H), 7.27 (d, J=6.97 Hz, 1H), 7.35 (t, J=7.63 Hz, 2H), 7.39-7.46 (m, 2H), 8.31 (brs, 2H), 8.75-8.86 (m, 4H), 8.93 (s, 1H), 9.00 (s, 1H), 9.02 (d, J=1.88 Hz, 1H), 9.30 (s, 1H), 10.21 (brs, 1H); ESIMS found for $C_{30}H_{21}N_9O$ m/z 524.2 (M+1).

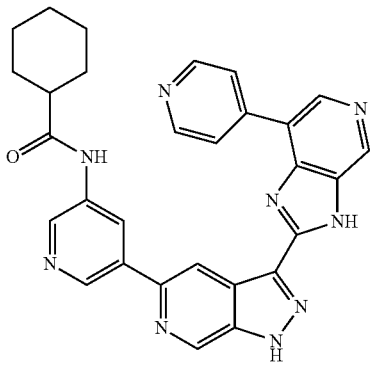
121



N-(5-(3-(7-(Pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 121.

White solid (12.5 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm 1.01 (t, J=7.44 Hz, 3H), 1.74 (sxt, J=7.32 Hz, 3H), 2.43 (t, J=7.35 Hz, 4H), 8.37 (brs, 3H), 8.73-8.83 (m, 3H), 8.86 (brs, 1H), 8.93 (brs, 1H), 9.01 (brs, 2H), 9.32 (d, J=1.13 Hz, 1H), 9.95 (brs, 1H), 14.28 (brs, 2H); ESIMS found for $C_{26}H_{21}N_9O$ m/z 476.1 (M+1).

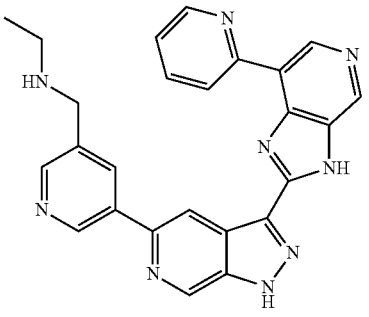
126



N-(5-(3-(7-(Pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide 126.

White solid (41.8 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm 1.22-1.45 (m, 3H), 1.47-1.64 (m, 2H), 1.69 (dd, J=8.01, 4.80 Hz, 1H), 1.76-1.87 (m, 2H), 1.88-1.99 (m, 2H), 8.37 (brs, 2H), 8.73-8.83 (m, 2H), 8.88 (brs, 1H), 8.92 (brs, 1H), 9.01 (brs, 2H), 9.31 (brs, 1H), 9.84 (brs, 1H); ESIMS found for $C_{29}H_{25}N_9O$ m/z 516.3 (M+1).

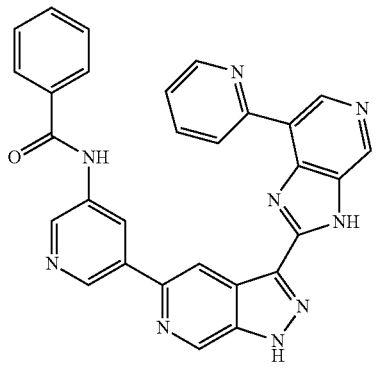
136



N-((5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine 136.

White solid (21.4 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.30 (t, J=7.22 Hz, 3H), 3.01-3.15 (m, 2H), 4.40 (d, J=5.02 Hz, 2H), 7.64 (dd, J=7.15, 5.27 Hz, 1H), 8.25 (t, J=6.84 Hz, 1H), 8.89 (d, J=3.76 Hz, 1H), 8.96 (brs, 1H), 9.06 (brs, 2H), 9.28 (s, 1H), 9.36 (brs, 1H), 9.43 (s, 1H), 9.48 (d, J=1.38 Hz, 1H), 9.62 (brs, 2H), 15.24 (brs, 1H); ESIMS found for $C_{25}H_{21}N_9$ m/z 448.0 (M+1).

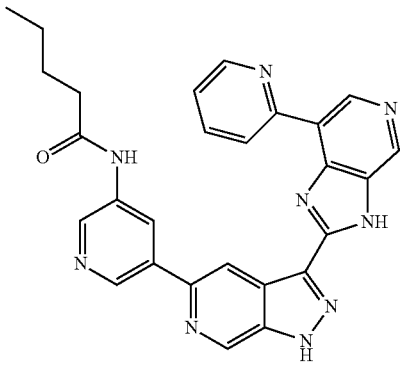
141



N-(5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide 141.

White solid (56.8 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.45 (brs, 1H), 7.58-7.65 (m, 2H), 7.67-7.74 (m, 1H), 8.13 (d, J=7.40 Hz, 2H), 8.23-8.31 (m, 1H), 8.81 (brs, 1H), 8.93 (s, 1H), 9.23 (s, 1H), 9.25 (s, 1H), 9.30 (brs, 2H), 9.37 (s, 1H), 9.49 (s, 1H), 11.29 (s, 1H), 15.25 (brs, 1H); ESIMS found for $C_{29}H_{19}N_9O$ m/z 510.1 (M+1).

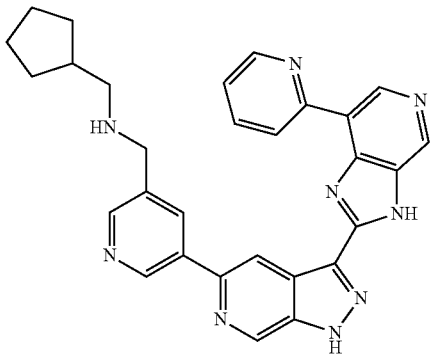
148



N-(5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 148.

White solid (27.0 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.94 (t, J=7.34 Hz, 3H), 1.38 (sxt, J=7.52 Hz, 2H), 1.65 (quin, J=7.16 Hz, 2H), 2.46 (t, J=7.68 Hz, 6H), 7.52-7.63 (m, 1H), 8.25 (brs, 1H), 8.87 (brs, 3H), 9.10 (brs, 2H), 9.27 (s, 2H), 9.38 (d, J=0.88 Hz, 1H), 10.68 (brs, 1H), 15.09 (brs, 1H); ESIMS found for $C_{27}H_{23}N_9O$ m/z 490.1 (M+1).

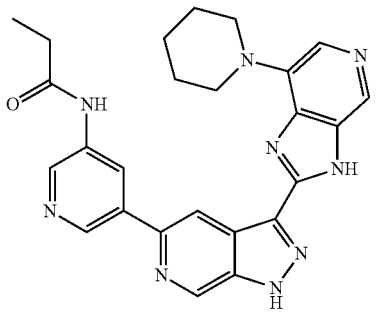
154



1-Cyclopentyl-N-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine 154.

White solid (23.6 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.20-1.36 (m, 2H), 1.47-1.67 (m, 4H), 1.76-1.89 (m, 2H), 2.27 (quin, J=7.80 Hz, 1H), 2.99 (q, J=4.40 Hz, 2H), 4.41 (t, J=4.64 Hz, 2H), 7.64 (dd, J=7.47, 5.58 Hz, 1H), 8.25 (brs, 1H), 8.90 (d, J=4.02 Hz, 1H), 8.95 (s, 1H), 9.05 (d, J=11.92 Hz, 2H), 9.29 (s, 1H), 9.42 (brs, 3H), 9.44 (d, J=1.00 Hz, 1H), 9.47 (s, 1H), 15.22 (brs, 1H); ESIMS found for $C_{29}H_{27}N_9$ m/z 502.2 (M+1).

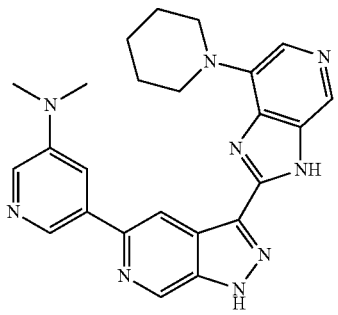
157



N-(5-(3-(7-(Piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide 157.

White solid (10.2 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.13 (t, J=7.53 Hz, 3H), 1.61 (brs, 6H), 2.42 (q, J=7.57 Hz, 2H), 3.49 (brs, 4H), 6.69 (s, 1H), 8.67 (s, 1H), 8.73 (d, J=1.63 Hz, 1H), 8.77 (s, 1H), 8.89 (d, J=1.51 Hz, 1H), 8.99 (s, 1H), 9.30 (s, 1H), 10.35 (s, 1H), 13.04 (s, 1H), 14.46 (brs, 1H); ESIMS found for $C_{25}H_{25}N_9O$ m/z 468.2 (M+1).

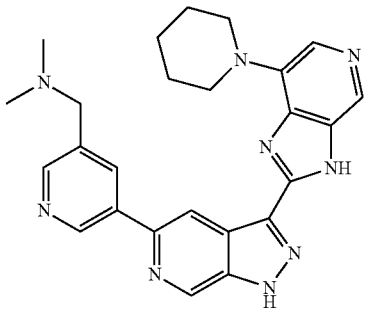
163



N,N-Dimethyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine 163.

White solid (17.6 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.67 (brs, 6H), 3.18 (s, 6H), 3.59 (brs, 4H), 7.13 (brs, 1H), 8.22 (brs, 1H), 8.30 (brs, 1H), 8.68 (brs, 2H), 8.89 (s, 1H), 9.32 (s, 1H), 15.12 (brs, 1H); ESIMS found for $C_{24}H_{25}N_9$ m/z 440.2 (M+1).

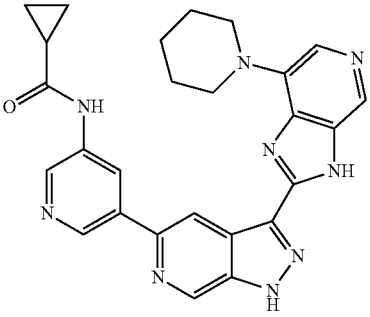
169



N,N-Dimethyl-1-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine 169.

White solid (13.5 mg, 0.03 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.75-1.87 (m, 6H), 3.03 (s, 6H), 3.60-3.66 (m, 4H), 4.69 (s, 2H), 7.28 (s, 1H), 8.62 (s, 1H), 8.99 (brs, 1H), 9.19 (s, 1H), 9.33 (brs, 1H), 9.35 (d, J=1.25 Hz, 1H), 9.65 (brs, 1H); ESIMS found for $C_{25}H_{27}N_9$ m/z 454.2 (M+1).

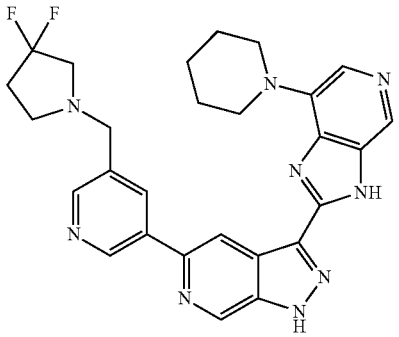
175



N-(5-(3-(7-(Piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide 175.

White solid (39.5 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.88-0.99 (m, 4H), 1.68 (brs, 6H), 1.91-2.03 (m, 1H), 3.33-3.46 (m, 4H), 7.14 (brs, 1H), 8.73 (s, 1H), 8.83 (d, J=0.88 Hz, 1H), 9.14 (s, 1H), 9.19 (d, J=6.78 Hz, 2H), 9.38 (d, J=1.00 Hz, 1H), 11.48 (s, 1H), 15.03 (brs, 1H); ESIMS found for $C_{26}H_{25}N_9O$ m/z 480.1

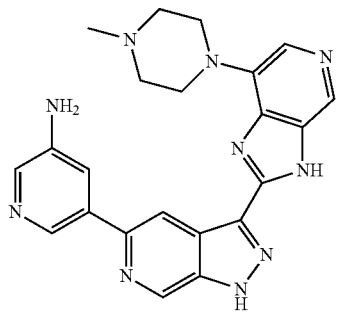
181



5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 181.

White solid (39.5 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.68 (brs, 6H), 2.57-2.71 (m, 2H), 3.60 (brs, 6H), 3.82-3.95 (m, 2H), 4.66 (brs, 2H), 7.16 (brs, 1H), 8.71 (s, 1H), 8.95 (s, 1H), 8.98 (s, 1H), 9.05 (s, 1H), 9.40 (d, J=0.75 Hz, 1H), 9.47 (d, J=1.76 Hz, 1H), 15.03 (brs, 1H); ESIMS found for $C_{27}H_{27}F_2N_9$ m/z 516.2 (M+1).

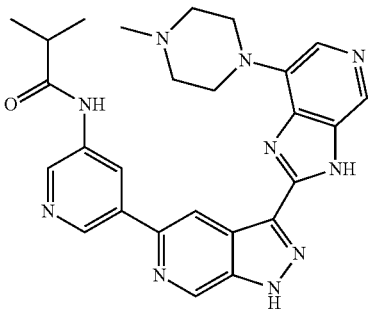
211



5-(3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine 211.

White solid (16.6 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.82 (brs, 3H), 3.10-3.23 (m, 4H), 3.55 (brs, 2H), 4.35 (d, J=12.55 Hz, 2H), 7.05 (brs, 1H), 8.08 (d, J=2.13 Hz, 1H), 8.39 (s, 1H), 8.70 (s, 1H), 8.75 (s, 1H), 8.87 (s, 1H), 9.35 (d, J=1.00 Hz, 1H), 11.18 (brs, 1H), 14.91 (brs, 1H); ESIMS found for $C_{22}H_{22}N_{10}$ m/z 427.1 (M+1).

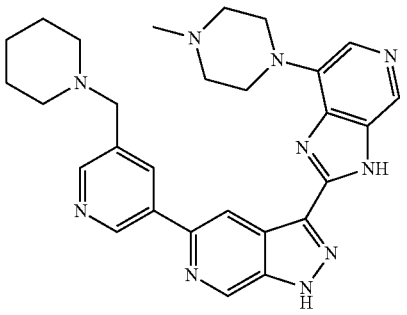
217



N-(5-(3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide 217.

White solid (20.5 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.19 (d, J=6.78 Hz, 6H), 2.81 (spt, J=6.92 Hz, 1H), 2.86 (brs, 3H), 3.21-3.33 (m, 2H), 3.49-3.62 (m, 4H), 4.33 (d, J=12.92 Hz, 2H), 7.16 (s, 1H), 8.72 (s, 1H), 8.79 (s, 1H), 9.19-9.24 (m, 2H), 9.27 (d, J=1.64 Hz, 1H), 9.29 (d, J=0.88 Hz, 1H), 11.30 (s, 1H), 11.44 (brs, 1H), 15.07 (brs, 1H); ESIMS found for $C_{26}H_{28}N_{10}O$ m/z 497.2 (M+1).

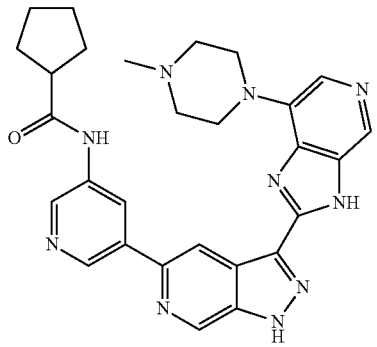
223



3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 223.

White solid (22.7 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.33-1.46 (m, 1H), 1.66-1.75 (m, 1H), 1.82 (brs, 4H), 2.84 (d, J=3.64 Hz, 3H), 2.92-3.04 (m, 2H), 3.18-3.30 (m, 2H), 3.42 (d, J=12.17 Hz, 2H), 3.49-3.62 (m, 4H), 4.34 (d, J=13.43 Hz, 2H), 4.56 (d, J=4.64 Hz, 2H), 7.22 (s, 1H), 8.79 (s, 1H), 9.02 (s, 1H), 9.06 (s, 1H), 9.18 (s, 1H), 9.39 (d, J=1.00 Hz, 1H), 9.52 (d, J=1.76 Hz, 1H), 11.16 (brs, 1H), 11.43 (brs, 1H), 15.11 (brs, 1H); ESIMS found for $C_{28}H_{32}$No m/z 509.2 (M+1).

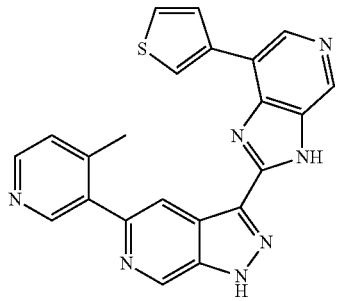
229



N-(5-(3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide 229.

White solid (13.3 mg, 0.03 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.64-1.76 (m, 2H), 1.77-1.86 (m, 2H), 1.88-1.99 (m, 2H), 2.00-2.11 (m, 2H), 2.99 (q, J=7.92 Hz, 1H), 3.05 (s, 2H), 3.43 (brs, 2H), 3.60 (brs, 2H), 3.75 (brs, 2H), 4.28 (brs, 2H), 7.46 (s, 1H), 8.83 (s, 1H), 9.14 (s, 1H), 9.29-9.33 (m, 2H), 9.34 (d, J=1.26 Hz, 1H), 9.42 (d, J=1.76 Hz, 1H); ESIMS found for $C_{28}H_{30}N_{10}O$ m/z 523.2 (M+1).

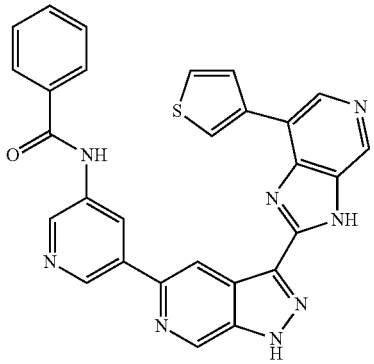
239



5-(4-Methylpyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 239.

White solid (21.0 mg, 0.05 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.87 (s, 3H), 7.73 (dd, J=5.08, 2.95 Hz, 1H), 8.05 (d, J=4.89 Hz, 1H), 8.18 (d, J=6.02 Hz, 1H), 8.82 (d, J=6.02 Hz, 2H), 8.88-8.94 (m, 2H), 9.13 (d, J=6.15 Hz, 2H), 9.43 (d, J=1.25 Hz, 1H); ESIMS found for $C_{22}H_{15}N_7S$ m/z 410.0 (M+1).

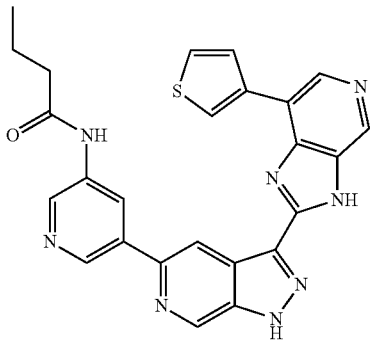
245



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide 245.

White solid (42.8 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.58-7.65 (m, 2H), 7.65-7.72 (m, 1H), 7.86 (dd, J=5.08, 2.95 Hz, 1H), 8.11-8.17 (m, 2H), 8.22 (brs, 1H), 8.95-9.05 (m, 3H), 9.11 (brs, 1H), 9.24 (s, 2H), 9.42 (d, J=1.00 Hz, 1H), 9.44 (brs, 1H), 11.13 (s, 1H), 15.18 (brs, 1H); ESIMS found for $C_{28}H_{18}N_8OS$ m/z 515.0 (M+1).

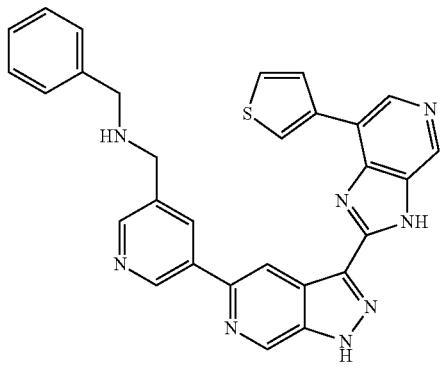
251



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 251.

White solid (32.2 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.98 (t, J=7.40 Hz, 3H), 1.71 (sxt, J=7.40 Hz, 2H), 2.47 (t, J=7.40 Hz, 4H), 7.91 (dd, J=4.83, 2.95 Hz, 1H), 8.23 (brs, 1H), 8.95 (s, 2H), 9.03 (d, J=4.77 Hz, 2H), 9.11 (brs, 1H), 9.19 (d, J=1.38 Hz, 1H), 9.27 (brs, 1H), 9.40 (d, J=0.63 Hz, 1H), 11.01 (brs, 1H), 15.19 (brs, 1H); ESIMS found for $C_{25}H_{20}N_8OS$ m/z 481.1 (M+1).

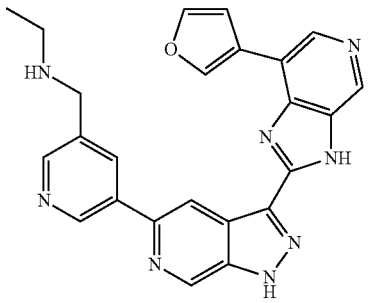
257



N-Benzyl-1-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine 257.

White solid (18.1 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 4.31 (brs, 2H), 4.46 (brs, 2H), 7.39-7.50 (m, 3H), 7.64 (dd, J=7.72, 1.69 Hz, 2H), 7.87 (dd, J=5.08, 2.95 Hz, 1H), 8.22 (brs, 1H), 8.68 (brs, 2H), 8.95 (s, 1H), 9.03 (brs, 3H), 9.05-9.17 (m, 2H), 9.41 (d, J=1.13 Hz, 1H), 9.46 (d, J=2.01 Hz, 1H), 10.10 (brs, 2H), 15.26 (brs, 2H); ESIMS found for $C_{29}H_{22}N_8S$ m/z 515.1 (M+1).

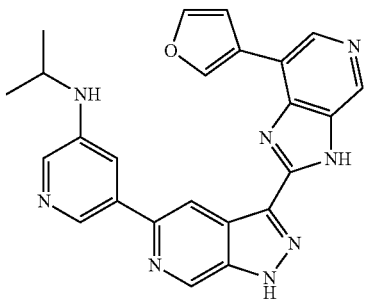
266



N-((5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine 266.

White solid (34.5 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.30 (t, J=7.22 Hz, 3H), 3.02-3.16 (m, 2H), 4.39 (t, J=5.52 Hz, 2H), 7.56 (brs, 1H), 8.01 (t, J=1.57 Hz, 1H), 8.93 (s, 1H), 8.96 (s, 1H), 9.01 (brs, 1H), 9.04 (s, 1H), 9.13 (d, J=8.91 Hz, 2H), 9.43 (d, J=0.88 Hz, 1H), 9.47 (d, J=1.63 Hz, 1H), 9.54 (brs, 2H), 15.22 (brs, 2H); ESIMS found for $C_{24}H_{20}N_8O$ m/z 437.1 (M+1).

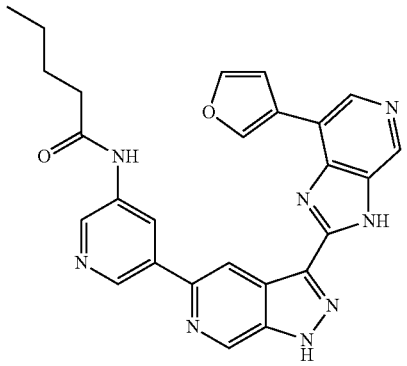
272



5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine 272.

White solid (45.5 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.23 (d, J=6.27 Hz, 6H), 3.67-3.80 (m, 1H), 5.94 (d, J=7.91 Hz, 1H), 7.44 (s, 1H), 7.59 (s, 1H), 7.90 (t, J=1.63 Hz, 1H), 8.04 (brs, 1H), 8.52 (brs, 1H), 8.74 (brs, 1H), 8.80 (brs, 1H), 8.88 (s, 1H), 8.91 (s, 1H), 9.33 (s, 1H), 13.79 (brs, 1H), 14.53 (brs, 1H); ESIMS found for $C_{24}H_{20}N_8O$ m/z 437.1 (M+1).

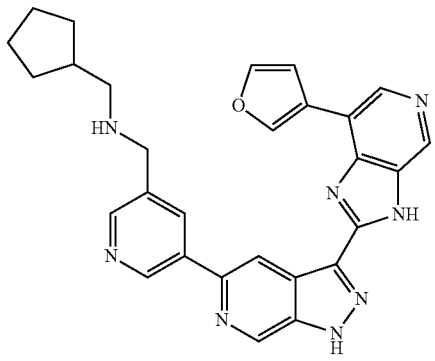
278



N-(5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 278.

White solid (25.5 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.34 Hz, 3H), 1.38 (sxt, J=7.56 Hz, 2H), 1.65 (quin, J=7.40 Hz, 2H), 2.45 (t, J=7.56 Hz, 4H), 7.58 (brs, 1H), 7.99 (t, J=1.69 Hz, 1H), 8.95 (s, 3H), 9.06 (brs, 1H), 9.14 (brs, 2H), 9.16 (s, 1H), 9.42 (d, J=1.00 Hz, 1H), 10.73 (brs, 1H), 15.13 (brs, 1H); ESIMS found for $C_{26}H_{22}N_8O_2$ m/z 479.1 (M+1).

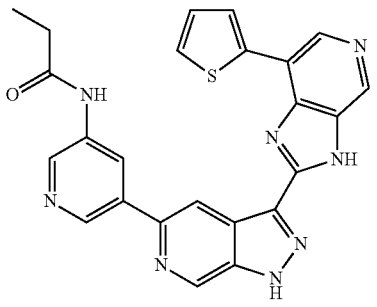
284



1-Cyclopentyl-N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine 284.

White solid (20.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.22-1.35 (m, 2H), 1.45-1.68 (m, 4H), 1.76-1.88 (m, 2H), 2.30 (spt, J=7.52 Hz, 1H), 2.97-3.05 (m, 2H), 4.44 (t, J=5.40 Hz, 4H), 7.56 (s, 1H), 7.99 (t, J=1.57 Hz, 1H), 8.96 (s, 1H), 9.06 (s, 2H), 9.09 (brs, 1H), 9.13 (brs, 1H), 9.21 (brs, 1H), 9.41 (d, J=0.88 Hz, 1H), 9.53 (d, J=1.38 Hz, 1H), 9.63 (brs, 2H), 15.30 (brs, 1H); ESIMS found for $C_{28}H_{26}N_8O$ m/z 491.2 (M+1).

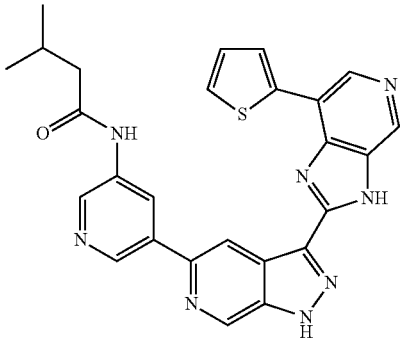
287



N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide 287.

White solid (15.1 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.17 (t, J=7.53 Hz, 3H), 2.47 (q, J=7.64 Hz, 4H), 7.34 (dd, J=5.02, 3.76 Hz, 1H), 7.80 (dd, J=5.12 Hz, J=0.88 Hz, 1H), 8.26 (brs, 1H), 8.71 (d, J=1.63 Hz, 1H), 8.84 (s, 1H), 8.88 (s, 1H), 9.04 (brs, 1H), 9.07 (d, J=2.01 Hz, 1H), 9.08 (s, 1H), 9.37 (d, J=1.25 Hz, 1H), 10.33 (s, 1H), 14.65 (brs, 1H); ESIMS found for $C_{24}H_{18}N_8OS$ m/z 467.0 (M+1).

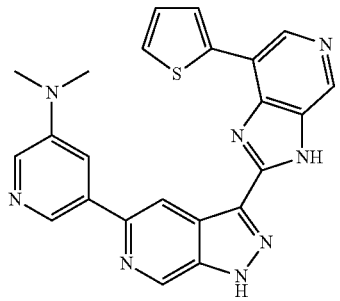
288



3-Methyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide 288.

Light brown solid (2.8 mg, 0.006 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.00 (d, J=6.5 Hz, 6H), 2.17 (non, J=7 Hz, 1H), 2.32 (d, J=7 Hz, 2H), 7.32 (dd, J=3.5 Hz, J=5 Hz, 1H), 7.75 (dd, J=1 Hz, J=5 Hz, 1H), 8.25 (d, J=2.5 Hz, 1H), 8.73 (s, 1H), 8.79 (s, 1H), 8.84 (s, 1H), 9.01 (s, 1H), 9.06 (s, 1H), 9.09 (s, 1H), 9.36 (s, 1H), 10.29 (s, 1H), 13.87 (brs, 1H), 14.57 (brs, 1H); ESIMS found for $C_{26}H_{22}N_8OS$ m/z 495.0 (M+1).

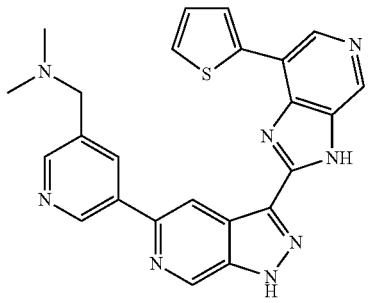
293



N,N-Dimethyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine 293.

White solid (15.8 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.13 (s, 6H), 7.21-7.25 (m, 1H), 7.93 (d, J=4.89 Hz, 1H), 8.02 (brs, 1H), 8.17 (dd, J=7.34, 2.95 Hz, 2H), 8.37 (s, 1H), 8.78 (s, 1H), 8.89 (s, 1H), 8.96 (s, 1H), 9.14 (s, 1H), 15.02 (brs, 1H); ESIMS found for $C_{23}H_{18}N_8S$ m/z 439.0 (M+1).

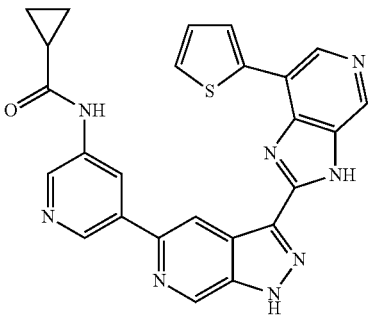
299



N,N-Dimethyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine 299.

White solid (13.0 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.83 (s, 6H), 4.59 (s, 2H), 7.33-7.39 (m, 1H), 8.03 (d, J=4.89 Hz, 1H), 8.34 (d, J=3.01 Hz, 1H), 9.00-9.11 (m, 5H), 9.37 (s, 1H), 9.39 (s, 1H), 11.33 (brs, 1H), 15.24 (brs, 1H); ESIMS found for $C_{24}H_{20}N_8S$ m/z 453.1 (M+1).

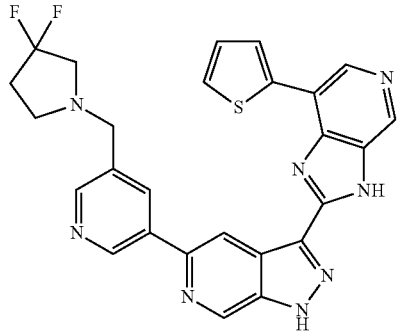
305



N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide 305.

White solid (21.4 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.89-0.99 (m, 4H), 1.92-2.01 (m, 1H), 7.37 (dd, J=5.02, 3.76 Hz, 1H), 7.97 (dd, J=5.08, 0.94 Hz, 1H), 8.33 (d, J=3.26 Hz, 1H), 8.94 (s, 1H), 9.02 (s, 1H), 9.04-9.11 (m, 3H), 9.20 (s, 1H), 9.38 (d, J=1.13 Hz, 1H), 11.21 (s, 1H), 15.10 (brs, 1H); ESIMS found for $C_{25}H_{18}N_8OS$ m/z 479.2 (M+1).

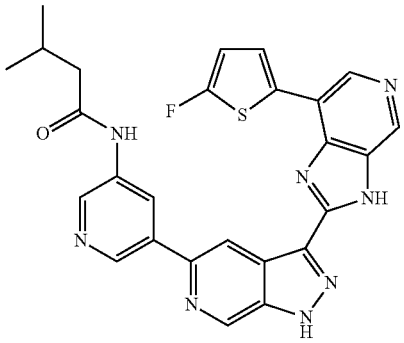
311



5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 311.

White solid (49.7 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.57-2.71 (m, 2H), 3.63 (brs, 2H), 3.92 (t, J=11.61 Hz, 2H), 4.72 (brs, 2H), 7.33-7.40 (m, 1H), 8.06 (d, J=4.77 Hz, 1H), 8.35 (d, J=2.76 Hz, 1H), 9.03 (s, 1H), 9.06 (s, 1H), 9.09 (brs, 1H), 9.10 (brs, 1H), 9.15 (brs, 1H), 9.38 (d, J=4.39 Hz, 2H), 15.26 (brs, 1H); ESIMS found for $C_{26}H_{20}F_2N_8S$ m/z 515.1 (M+1).

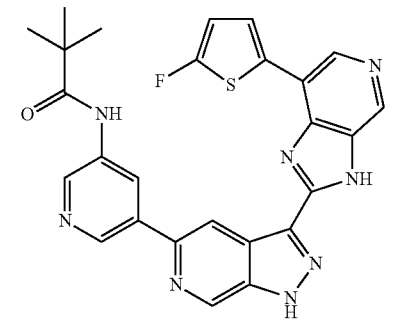
314



N-(5-(3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 314.

White solid (32.3 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.98 (d, J=6.65 Hz, 6H), 2.09-2.20 (m, 1H), 2.33 (d, J=7.15 Hz, 2H), 6.98 (dd, J=4.27, 1.88 Hz, 1H), 8.00 (t, J=3.64 Hz, 1H), 8.88 (s, 1H), 8.97 (brs, 2H), 9.02 (s, 1H), 9.03 (s, 1H), 9.11 (s, 1H), 9.31 (d, J=0.88 Hz, 1H), 10.81 (brs, 1H), 15.09 (brs, 1H); ESIMS found for $C_{26}H_{21}FN_8OS$ m/z 513.1

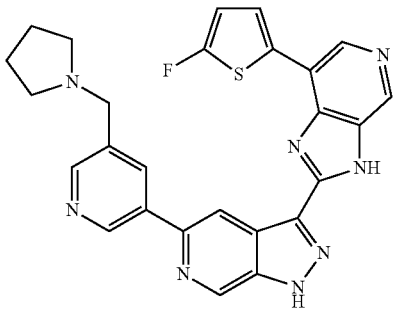
320



N-(5-(3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide 320.

White solid (32.1 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.31 (s, 9H), 6.95 (dd, J=4.08, 1.69 Hz, 1H), 7.99 (t, J=3.76 Hz, 1H), 8.85 (s, 1H), 8.94 (s, 1H), 8.99 (s, 1H), 9.05 (s, 1H), 9.16 (s, 1H), 9.25 (s, 1H), 9.29 (s, 1H), 10.18 (s, 1H), 15.11 (brs, 1H); ESIMS found for $C_{26}H_{21}FN_8OS$ m/z 513.1 (M+1).

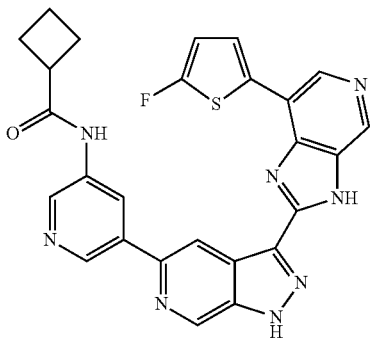
326



3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 326.

White solid (10.6 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.92 (brs, 2H), 2.07 (brs, 2H), 3.12-3.23 (m, 5H), 4.56 (brs, 2H), 6.97 (dd, J=4.27, 1.76 Hz, 1H), 7.97 (t, J=3.70 Hz, 1H), 8.82 (s, 1H), 8.93 (s, 2H), 8.97 (s, 1H), 9.06 (s, 1H), 9.30 (brs, 2H), 11.25 (brs, 1H), 15.11 (brs, 1H); ESIMS found for $C_{26}H_{21}FN_8S$ m/z 497.1 (M+1).

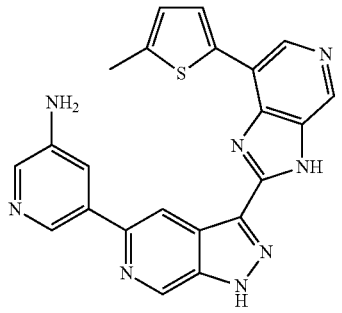
332



N-(5-(3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide 332.

White solid (6.8 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.80-1.91 (m, 1H), 1.95-2.06 (m, 1H), 2.13-2.24 (m, 2H), 2.25-2.35 (m, 2H), 3.25-3.37 (m, 1H), 6.99-7.05 (m, 1H), 8.05 (t, J=3.52 Hz, 1H), 8.90 (s, 1H), 9.00 (s, 1H), 9.04 (s, 1H), 9.06 (s, 2H), 9.15 (s, 1H), 9.38 (s, 1H), 10.51 (s, 1H), 15.08 (brs, 1H); ESIMS found for $C_{26}H_{19}FN_8OS$ m/z 511.1 (M+1).

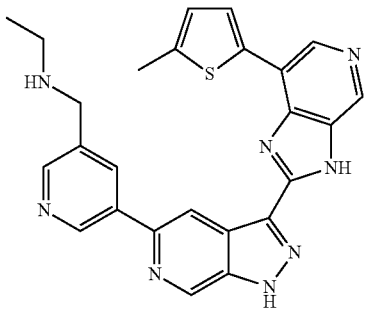
341



5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine 341.

White solid (30.8 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.64 (s, 3H), 7.09 (dd, J=3.52 Hz, J=0.88 Hz, 1H), 8.12 (d, J=2.38 Hz, 1H), 8.17 (d, J=2.64 Hz, 1H), 8.33 (s, 1H), 8.62 (s, 1H), 9.00 (s, 1H), 9.04 (s, 1H), 9.06 (s, 1H), 9.42 (d, J=1.00 Hz, 1H), 15.14 (brs, 1H); ESIMS found for $C_{22}H_{16}N_8S$ m/z 425.1 (M+1).

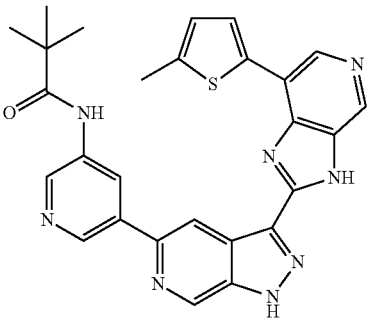
344



N-((5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine 344.

White solid (52.9 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.31 (t, J=7.22 Hz, 3H), 2.57 (s, 3H), 3.03-3.14 (m, 2H), 4.38 (t, J=5.77 Hz, 2H), 6.94 (d, J=2.64 Hz, 1H), 8.00 (d, J=3.51 Hz, 1H), 8.85 (s, 1H), 8.87 (s, 1H), 8.92 (brs, 2H), 8.97 (s, 1H), 9.21 (s, 1H), 9.25 (s, 1H), 9.64 (brs, 2H), 14.98 (brs, 1H), 15.07 (brs, 1H); ESIMS found for $C_{25}H_{22}N_8S$ m/z 467.2 (M+1).

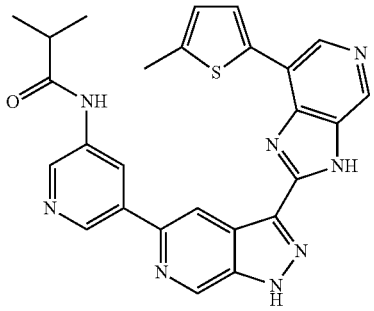
346



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide 346.

White solid (18.2 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.29 (s, 9H), 2.61 (s, 3H), 7.01 (d, J=2.38 Hz, 1H), 8.05 (d, J=3.14 Hz, 1H), 8.75 (s, 2H), 8.94 (s, 2H), 9.09 (s, 1H), 9.21 (s, 1H), 9.35 (d, J=1.13 Hz, 1H), 9.64 (s, 1H); ESIMS found for $C_{27}H_{24}N_8OS$ m/z 509.1 (M+1).

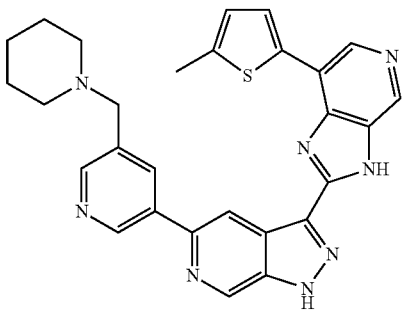
347



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide 347.

White solid (36.1 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.18 (d, J=6.78 Hz, 6H), 2.61 (s, 3H), 2.74 (spt, J=6.78 Hz, 1H), 7.05 (dd, J=3.64, 1.00 Hz, 1H), 8.13 (d, J=3.39 Hz, 1H), 8.95 (s, 1H), 8.97 (brs, 1H), 9.00 (d, J=2.01 Hz, 1H), 9.05 (d, J=1.88 Hz, 2H), 9.08 (s, 1H), 9.35 (d, J=1.13 Hz, 1H), 10.70 (brs, 1H), 15.04 (brs, 1H), 15.08 (brs, 1H); ESIMS found for $C_{26}H_{22}N_8OS$ m/z 495.1 (M+1).

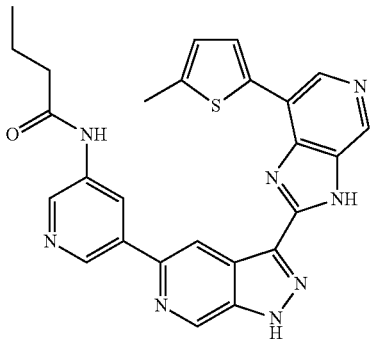
353



3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 353.

White solid (25.2 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.36-1.56 (m, 2H), 1.57-1.78 (m, 4H), 2.65 (s, 3H), 2.89 (brs, 2H), 4.15 (brs, 2H), 6.98 (d, J=1.76 Hz, 1H), 8.00 (d, J=2.13 Hz, 1H), 8.68 (brs, 2H), 8.76 (d, J=7.15 Hz, 2H), 9.29 (brs, 1H), 9.36 (brs, 1H), 9.40 (brs, 1H), 13.86 (brs, 1H), 14.55 (brs, 1H); ESIMS found for $C_{28}H_{26}N_8S$ m/z 507.2 (M+1).

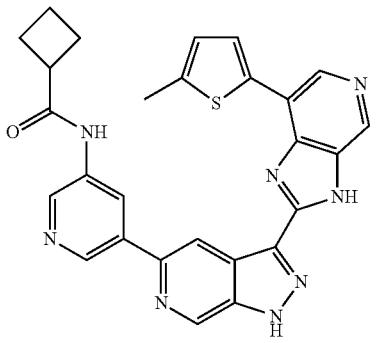
355



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 355.

White solid (59.2 mg, 0.12 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.96 (t, J=7.40 Hz, 3H), 1.68 (sxt, J=7.40 Hz, 2H), 2.39 (t, J=7.28 Hz, 2H), 2.61 (s, 3H), 6.98-7.03 (m, 1H), 8.01 (d, J=3.39 Hz, 1H), 8.75 (d, J=3.39 Hz, 2H), 8.79 (d, J=2.38 Hz, 1H), 8.95 (s, 1H), 9.08 (d, J=1.88 Hz, 1H), 9.20 (s, 1H), 9.35 (d, J=1.00 Hz, 1H), 10.30 (s, 1H); ESIMS found for $C_{26}H_{22}N_8OS$ m/z 495.1 (M+1).

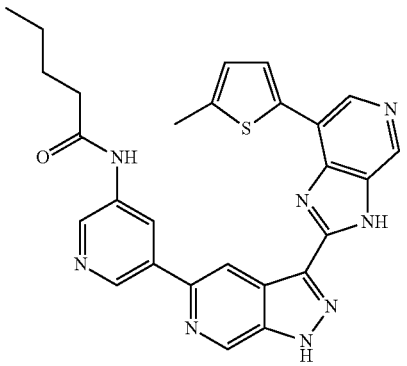
358



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide 358.

White solid (44.2 mg, 0.09 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.81-1.92 (m, 1H), 1.96-2.07 (m, 1H), 2.14-2.25 (m, 2H), 2.25-2.35 (m, 2H), 2.59 (s, 3H), 3.32-3.42 (m, 1H), 7.05 (d, J=3.64 Hz, 1H), 8.12 (d, J=3.14 Hz, 1H), 8.94 (s, 1H), 8.97 (s, 1H), 9.01 (d, J=1.76 Hz, 1H), 9.03 (s, 1H), 9.05 (d, J=1.63 Hz, 1H), 9.10 (s, 1H), 9.35 (d, J=1.00 Hz, 1H), 10.64 (s, 1H), 15.05 (brs, 1H); ESIMS found for $C_{27}H_{22}N_8OS$ m/z 507.1 (M+1).

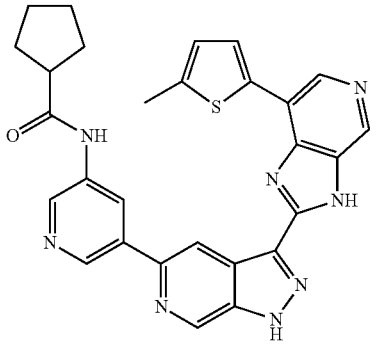
356



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 356.

White solid (74.7 mg, 0.15 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.92 (t, J=7.34 Hz, 3H), 1.37 (sxt, J=7.28 Hz, 2H), 1.63 (quin, J=7.68 Hz, 2H), 2.41 (t, J=7.40 Hz, 2H), 2.62 (s, 3H), 7.03 (d, J=2.64 Hz, 1H), 8.05 (d, J=3.39 Hz, 1H), 8.78 (d, J=2.26 Hz, 1H), 8.86 (d, J=3.64 Hz, 2H), 8.95 (s, 1H), 9.06 (d, J=1.51 Hz, 1H), 9.17 (s, 1H), 9.36 (d, J=1.00 Hz, 1H), 10.31 (s, 1H), 14.68 (brs, 1H); ESIMS found for $C_{27}H_{24}N_8OS$ m/z 509.1 (M+1).

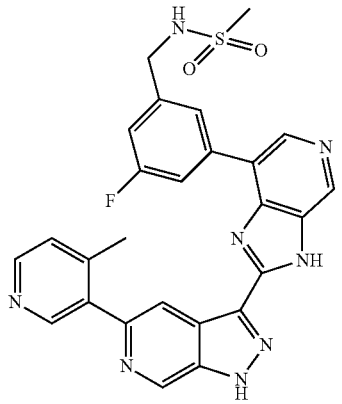
359



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide 359.

White solid (28.4 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.55-1.65 (m, 2H), 1.65-1.83 (m, 4H), 1.87-1.98 (m, 2H), 2.63 (s, 3H), 2.83-2.93 (m, 1H), 7.04 (d, J=3.26 Hz, 1H), 8.09 (d, J=3.51 Hz, 1H), 8.82 (d, J=2.26 Hz, 1H), 8.91 (d, J=3.51 Hz, 2H), 8.98 (s, 1H), 9.05 (s, 1H), 9.16 (s, 1H), 9.36 (s, 1H), 10.34 (s, 1H), 14.79 (s, 1H); ESIMS found for $C_{28}H_{24}N_8OS$ m/z 521.1 (M+1).

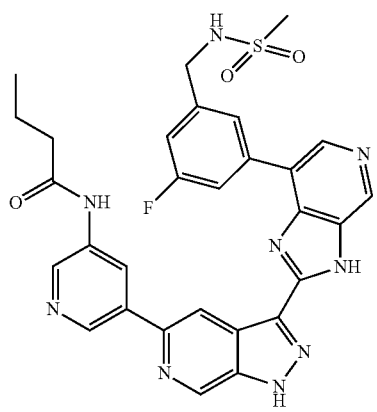
395



N-(3-Fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide 395.

White solid (9.5 mg, 0.02 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.77 (s, 3H), 2.87 (s, 3H), 4.36 (s, 2H), 7.37 (d, J=8.91 Hz, 1H), 7.95 (d, J=9.16 Hz, 1H), 8.13 (brs, 1H), 8.15 (d, J=6.15 Hz, 1H), 8.79-8.84 (m, 2H), 8.86 (d, J=1.13 Hz, 1H), 9.05 (s, 1H), 9.25 (s, 1H), 9.44 (d, J=1.13 Hz, 1H); ESIMS found for $C_{26}H_{21}FN_8O_2S$ m/z 529.1 (M+1).

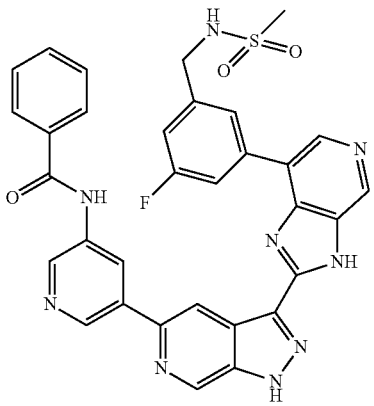
407



N-(5-(3-(7-(3-Fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide 407.

White solid (9.2 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.95 (t, J=7.40 Hz), 3H), 1.66 (sxt, J=7.35 Hz, 2H), 2.39 (t, J=7.28 Hz, 2H), 2.93 (s, 3H), 4.37 (d, J=6.27 Hz, 2H), 7.40 (d, J=9.29 Hz, H), 1H), 7.79 (t, J=6.34 Hz, 1H), 8.17 (brs, 1H), 8.38 (brs, 1H), 8.83 (d, J=2.01 Hz, 1H), 8.91 (d, J=5.15 Hz, 3H), 8.98 (d, J=1.76 Hz, 1H), 9.18 (brs, 1H), 9.40 (d, J=1.13 Hz, 1H), 10.37 (brs, 1H), 14.93 (brs, 1H); ESIMS found for $C_{29}H_{26}FN_9O_3S$ m/z 600.2 (M+1).

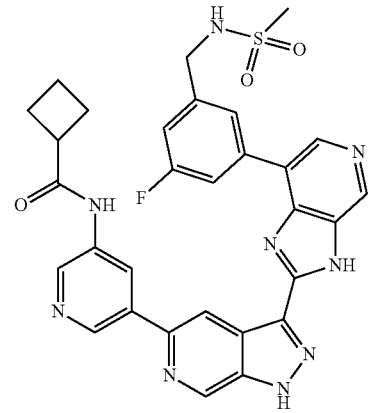
401



N-(5-(3-(7-(3-Fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide 401.

White solid (15.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.93 (s, 3H), 4.36 (d, J=6.40 Hz, 2H), 7.32 (brs, 1H), 7.57-7.65 (m, 2H), 7.65-7.72 (m, 1H), 7.78 (t, J=6.09 Hz, 1H), 8.08 (d, J=7.03 Hz, 2H), 8.85-8.97 (m, 1H), 8.98 (s, 1H), 9.16 (s, 1H), 9.19 (s, 1H), 9.21 (brs, 1H), 9.28 (s, 1H), 9.45 (d, J=1.00 Hz, 1H), 10.88 (brs, 1H), 15.10 (brs, 1H); ESIMS found for $C_{32}H_{24}FN_9O_3S$ m/z 634.1 (M+1).

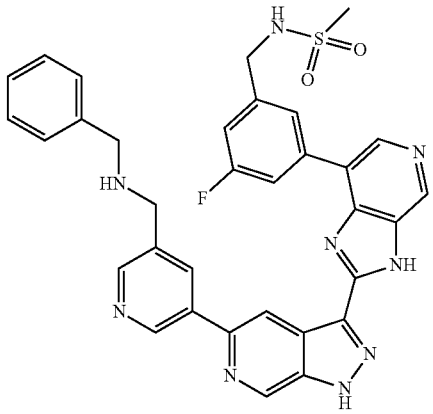
410



N-(5-(3-(7-(3-Fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide 410.

White solid (59.1 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.78-1.90 (m, 1H), 1.93-2.04 (m, 1H), 2.11-2.21 (m, 2H), 2.22-2.33 (m, 2H), 2.93 (s, 3H), 3.25-3.36 (m, 1H), 4.35 (d, J=6.27 Hz, 2H), 7.32 (d, J=9.03 Hz, 1H), 7.75 (t, J=6.27 Hz, 1H), 8.05 (brs, 1H), 8.29 (brs, 1H), 8.77 (brs, 1H), 8.83 (brs, 1H), 8.86 (brs, 1H), 8.91 (s, 1H), 8.96 (brs, 1H), 9.03 (brs, 1H), 9.35 (s, 1H), 10.11 (s, 1H), 14.65 (brs, 1H); ESIMS found for $C_{30}H_{26}FN_9O_3S$ m/z 612.2 (M+1).

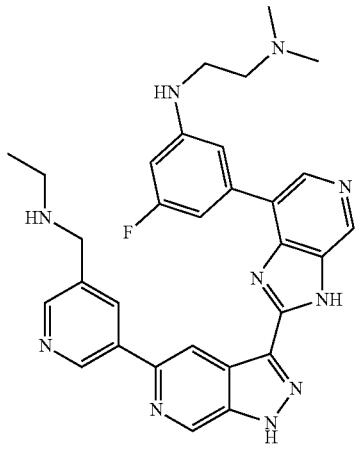
413



N-(3-(2-(5-(5-((Benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide 413.

White solid (25.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.95 (s, 3H), 4.22-4.32 (m, 2H), 4.40 (t, J=5.27 Hz, 4H), 7.37-7.50 (m, 4H), 7.54-7.64 (m, 2H), 7.84 (t, J=5.77 Hz, 1H), 8.18 (brs, 1H), 8.46 (brs, 1H), 8.85 (s, 2H), 8.98 (brs, 1H), 9.00 (s, 1H), 9.28 (brs, 1H), 9.39 (s, 1H), 9.43 (d, J=1.26 Hz, 1H), 9.77 (brs, 2H), 15.16 (brs, 1H), 15.32 (brs, 1H); ESIMS found for $C_{33}H_{28}FN_9O_2S$ m/z 634.2 (M+1).

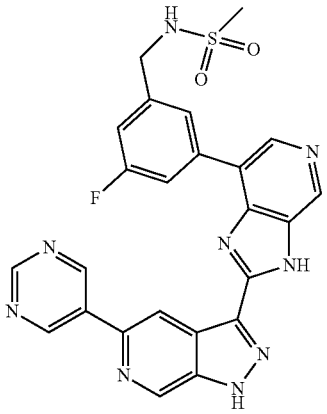
422



N-(3-(2-(5-(5-((Ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N2,N2-dimethylethane-1,2-diamine 422.

White solid (42.3 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.28 (t, J=7.22 Hz, 3H), 2.83 (s, 3H), 2.84 (s, 3H), 2.99-3.11 (m, 2H), 3.26-3.35 (m, 2H), 3.58-3.65 (m, 2H), 4.35 (brs, 2H), 6.73 (d, J=11.67 Hz, 1H), 8.91 (s, 3H), 9.03 (s, 1H), 9.26 (brs, 1H), 9.43 (s, 2H), 9.50 (brs, 2H), 10.68 (brs, 1H), 15.22 (brs, 1H); ESIMS found for $C_{30}H_{31}FN_{10}$ m/z 551.2 (M+1).

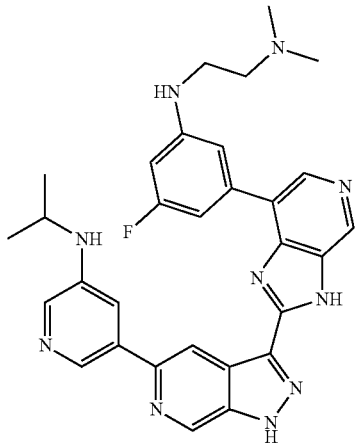
416



N-(3-Fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl) methanesulfonamide 416.

White solid (28.8 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.96 (s, 3H), 4.38 (d, J=6.02 Hz, 2H), 7.44 (d, J=9.16 Hz, 1H), 7.82 (t, J=6.34 Hz, 1H), 8.12 (brs, 1H), 8.36 (brs, 1H), 8.94 (s, 2H), 9.27 (s, 2H), 9.41 (s, 1H), 9.47 (s, 2H), 15.12 (brs, 1H); ESIMS found for $C_{24}H_{18}FN_9O_2S$ m/z 516.1 (M+1).

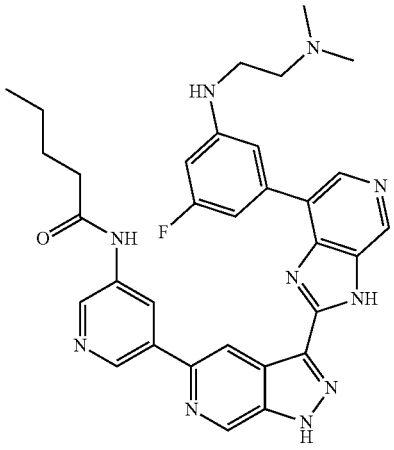
428



N^1-(3-Fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N2,N2-dimethylethane-1,2-diamine 428.

White solid (82.3 mg, 0.15 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.20 (d, J=6.27 Hz, 6H), 2.85 (s, 6H), 3.50-3.59 (m, 2H), 3.62-3.74 (m, 2H), 5.89 (brs, 1H), 6.37 (brs, 1H), 6.59 (d, J=11.42 Hz, 1H), 7.46 (brs, 2H), 7.67 (brs, 1H), 8.02 (brs, 1H), 8.50 (brs, 1H), 8.68 (brs, 1H), 8.89 (brs, 2H), 9.33 (s, 1H), 13.87 (brs, 1H), 14.54 (brs, 1H); ESIMS found for $C_{30}H_{31}FN_{10}$ m/z 551.3 (M+1).

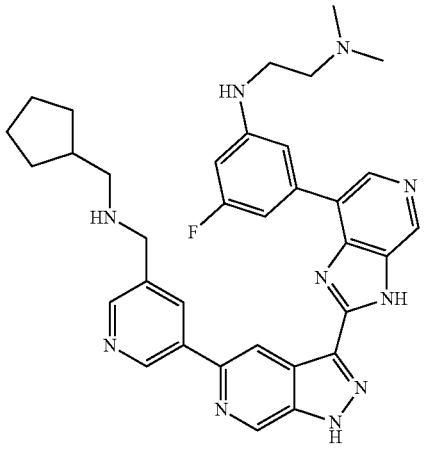
434



N-(5-(3-(7-(3-((2-(Dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide 434.

White solid (142.0 mg, 0.24 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.92 (t, J=7.34 Hz, 3H), 1.37 (sxt, J=7.40 Hz, 2H), 1.63 (quin, J=7.50 Hz, 2H), 2.46 (t, J=7.56 Hz, 2H), 2.82 (s, 3H), 2.83 (s, 3H), 3.30 (q, J=4.77 Hz, 2H), 3.61 (t, J=6.40 Hz, 2H), 6.69 (d, J=11.67 Hz, 1H), 7.42 (brs, 2H), 8.89 (brs, 1H), 8.97 (s, 1H), 9.12 (brs, 1H), 9.14 (brs, 1H), 9.17 (s, 1H), 9.26 (brs, 1H), 9.41 (s, 1H), 10.70 (brs, 1H), 10.98 (brs, 1H), 15.22 (brs, 1H); ESIMS found for $C_{32}H_{33}FN_{10}O$ m/z 593.2 (M+1).

440

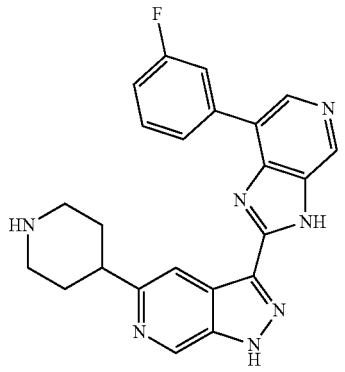


N^1-(3-(2-(5-(5-(((Cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N2,N2-dimethylethane-1,2-diamine 440.

White solid (40.3 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.21-1.33 (m, 2H), 1.44-1.67 (m, 4H), 1.74-1.87 (m, 2H), 2.28 (quin, J=8.00 Hz, 1H), 2.83 (d, J=4.64 Hz, 6H), 2.92-3.05 (m, 2H), 3.24-3.34 (m, 2H), 3.57-3.67 (m, 2H), 4.34-4.48 (m, 3H), 6.72 (d, J=11.67 Hz, 1H), 8.91 (d, J=1.63 Hz, 1H), 9.06 (s, 2H), 9.09-9.15 (m, 1H), 9.21-9.32 (m, 1H), 9.42 (d, J=1.00 Hz, 1H), 9.50 (d, J=1.63 Hz, 1H), 9.62 (brs, 2H), 10.84 (brs, 1H), 15.33 (brs, 1H);

ESIMS found for $C_{34}H_{37}FN_{10}$ m/z 605.2 (M+1).

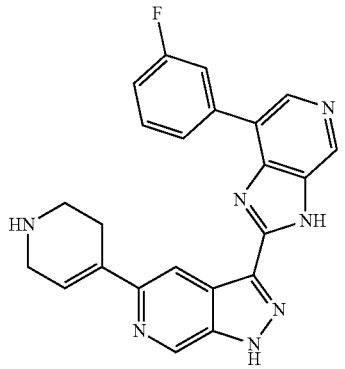
885



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine 885.

White solid (20.0 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.00 (br d, J=10.98 Hz, 2H), 2.22 (br s, 2H), 3.06-3.27 (m, 3H), 3.44 (br d, J=12.35 Hz, 2H), 7.32 (td, J=8.71, 2.61 Hz, 1H), 7.66 (br d, J=6.04 Hz, 1H), 8.22 (br s, 1H), 8.29 (s, 1H), 8.37 (br d, J=8.23 Hz, 1H), 8.45 (br s, 1H), 8.76 (br s, 1H), 9.18 (s, 1H), 13.85 (br s, 1H), 14.42 (br s, 1H); ESIMS found for $C_{23}H_{20}FN_7$ m/z 414.1 (M+1).

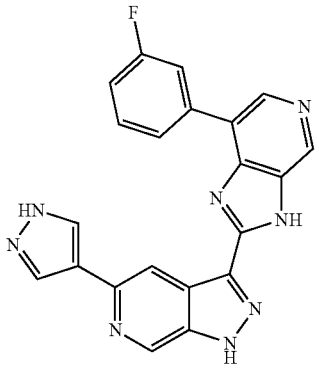
886



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine 886.

White solid (90.0 mg, 0.22 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.90 (br s, 2H), 3.42 (br t, J=6.04 Hz, 2H), 3.86 (br s, 2H), 6.90 (br s, 1H), 7.32 (td, J=8.44, 2.33 Hz, 1H), 7.58-7.67 (m, 1H), 8.13 (br s, 1H), 8.46 (br s, 1H), 8.57 (s, 1H), 8.76 (br s, 1H), 8.91 (s, 1H), 9.20 (d, J=1.10 Hz, 1H); ESIMS found for $C_{23}H_{18}FN_7$ m/z 412.1 (M+1).

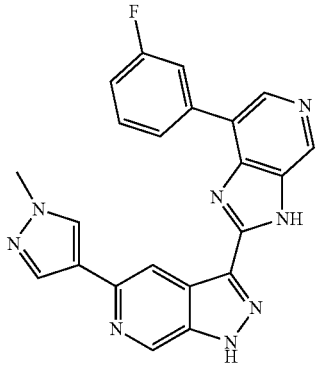
887



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine 887.

Brown solid (37.0 mg, 0.09 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.35 (td, J=8.44, 2.33 Hz, 1H), 7.61-7.70 (m, 1H), 8.14 (br s, 3H), 8.52 (br s, 1H), 8.60 (s, 1H), 8.75 (br s, 1H), 8.90 (s, 1H), 9.17 (d, J=1.10 Hz, 1H), 13.09 (brs, 1H), 13.93 (brs, 1H); ESIMS found for $C_{21}H_{13}FN_8$ m/z 397.1 (M+1).

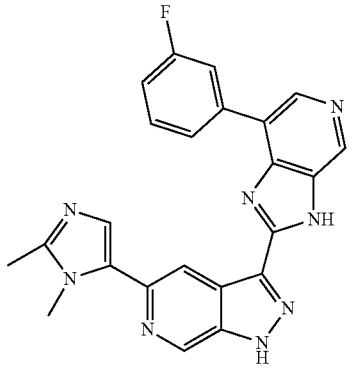
888



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine 888.

Yellow solid (10.7 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 3.94 (s, 3H), 7.35 (br t, J=8.64 Hz, 1H), 7.61-7.70 (m, 1H), 7.96 (s, 1H), 8.10 (br s, 1H), 8.22 (s, 1H), 8.49 (br s, 1H), 8.58 (s, 1H), 8.73 (br s, 1H), 8.89 (s, 1H), 9.16 (s, 1H), 13.87 (brs, 1H); ESIMS found for $C_{22}H_{15}FN_8$ m/z 411.1 (M+1).

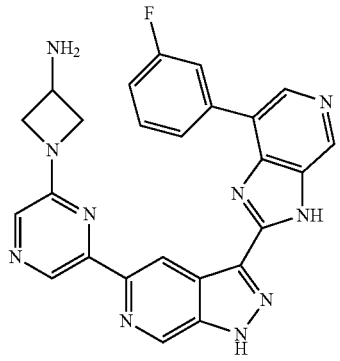
889



5-(1,2-Dimethyl-1H-imidazol-5-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 889.

Brown solid (16.4 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.38 (s, 3H), 3.82 (s, 3H), 7.05 (s, 1H), 7.18-7.26 (m, 1H), 7.50-7.59 (m, 1H), 8.15 (br d, J=7.96 Hz, 1H), 8.44 (br s, 1H), 8.48-8.55 (m, 2H), 8.68 (s, 1H), 9.06 (s, 1H); ESIMS found for $C_{23}H_{17}FN_8$ m/z 425.2 (M+1).

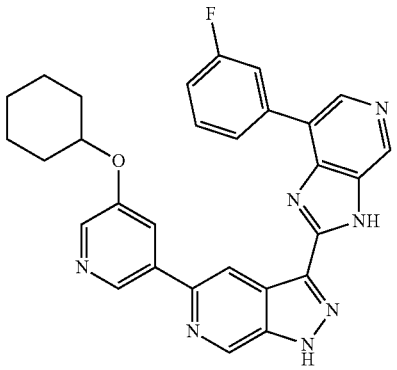
890



1-(6-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine 890.

Yellow solid (31.1 mg, 0.065 mmol, 63.3% yield). ^{1}H NMR (DMSO-do, 500 MHz) δ ppm 3.69-3.79 (m, 2H), 3.96 (dt, J=12.90, 6.17 Hz, 1H), 4.26 (br t, J=7.55 Hz, 2H), 7.32-7.42 (m, 1H), 7.59-7.69 (m, 1H), 7.89 (s, 1H), 8.00 (br d, J=10.15 Hz, 1H), 8.08 (br s, 1H), 8.61 (s, 1H), 8.84 (s, 1H), 8.90 (s, 1H), 9.21 (s, 1H), 9.27 (s, 1H); ESIMS found for $C_{25}H_{19}FN_1O$ m/z 479.1 (M+H).

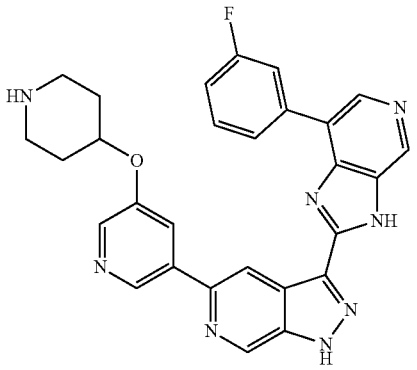
891



5-(5-(Cyclohexyloxy)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 891.

Brown solid (37 mg, 0.073 mmol, 12.4% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.26-1.38 (m, 1H), 1.38-1.49 (m, 2H), 1.50-1.62 (m, 3H), 1.69-1.81 (m, 2H), 1.93-2.05 (m, 2H), 4.53-4.63 (m, 1H), 7.30 (td, J=8.51, 2.47 Hz, 1H), 7.58-7.67 (m, 1H), 7.99 (t, J=2.20 Hz, 1H), 8.23 (br s, 1H), 8.35 (d, J=2.74 Hz, 1H), 8.42 (br s, 1H), 8.75 (br s, 1H), 8.90 (d, J=1.65 Hz, 2H), 8.96 (s, 1H), 9.34 (d, J=0.82 Hz, 1H), 13.97 (br s, 1H), 14.38 (br s, 1H); ESIMS found for $C_{29}H_{24}FN_7O$ m/z 506.2 (M+1).

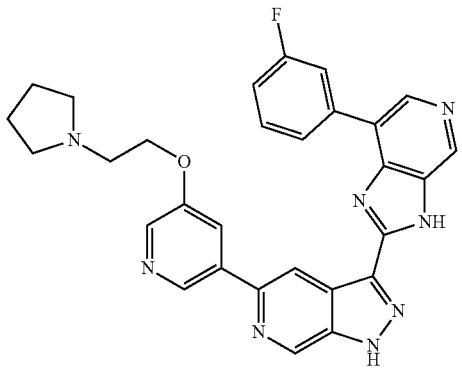
892



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 892.

Yellow solid (50 mg, 0.094 mmol, 64.8% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.88-2.01 (m, 2H), 2.12-2.23 (m, 2H), 3.11-3.21 (m, 2H), 3.26-3.36 (m, 2H), 4.92 (dt, J=7.14, 3.57 Hz, 1H), 7.37 (td, J=8.58, 2.33 Hz, 1H), 7.61-7.69 (m, 1H), 8.08 (t, J=2.06 Hz, 1H), 8.19 (br s, 1H), 8.45 (d, J=2.74 Hz, 1H), 8.59 (br s, 2H), 8.80 (br s, 1H), 8.96 (s, 2H), 9.00 (br s, 1H), 9.34 (d, J=1.10 Hz, 1H), 14.68 (br s, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.2 (M+1).

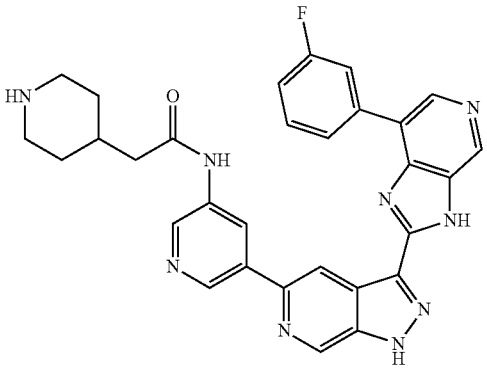
894



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 894.

Yellow solid (4.1 mg, 7.88 μmol, 10.35% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.75 (br s, 4H), 2.70 (br s, 4H), 3.01 (br s, 2H), 4.32 (br t, J=5.21 Hz, 2H), 7.28-7.35 (m, 1H), 7.60-7.68 (m, 1H), 8.05 (br s, 1H), 8.23 (br s, 1H), 8.38 (d, J=2.47 Hz, 1H), 8.42 (br s, 1H), 8.76 (br s, 1H), 8.88-8.96 (m, 2H), 8.98 (br s, 1H), 9.34 (s, 1H), 13.93 (brs, 2H); ESIMS found for $C_{29}H_{25}FN_8O$ m/z 521.2 (M+1).

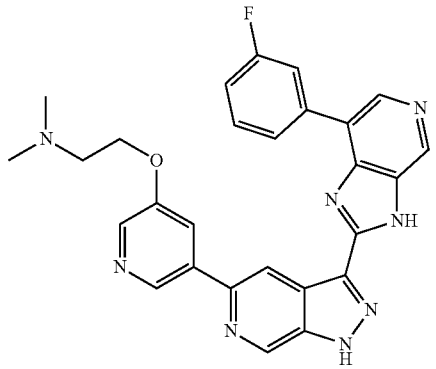
893



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide 893.

Yellow solid (8.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.02-1.14 (m, 1H), 1.16-1.24 (m, 1H), 1.69-1.82 (m, 2H), 2.02-2.12 (m, 1H), 2.37 (d, J=6.86 Hz, 2H), 2.52-2.61 (m, 1H), 2.99-3.08 (m, 1H), 3.81 (br d, J=13.72 Hz, 1H), 4.37 (br d, J=12.90 Hz, 1H), 7.35-7.43 (m, 1H), 7.66-7.76 (m, 1H), 8.21 (br s, 1H), 8.32 (br s, 1H), 8.80 (s, 1H), 8.85 (br s, 1H), 8.88-8.96 (m, 2H), 8.99 (d, J=1.65 Hz, 1H), 9.12 (br s, 1H), 9.38 (d, J=1.10 Hz, 1H), 10.32 (s, 1H), 14.75 (br s, 1H); ESIMS found for $C_{30}H_{26}FN_9O$ m/z 548.1 (M+1).

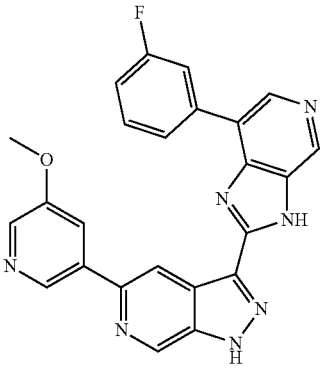
895



2-((5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine 895.

White solid (12.1 mg, 0.024 mmol, 20.82% yield). ^{1}H NMR (DMSO-d6, 500 MHz) δ ppm 2.27 (s, 6H), 2.73 (t, J=5.63 Hz, 2H), 4.26 (t, J=5.63 Hz, 2H), 7.31 (td, J=8.64, 2.20 Hz, 1H), 7.60-7.68 (m, 1H), 8.00-8.05 (m, 1H), 8.18 (br s, 1H), 8.36 (d, J=2.74 Hz, 1H), 8.73 (br s, 1H), 8.92 (br s, 1H), 8.93 (d, J=1.92 Hz, 1H), 8.96 (d, J=0.82 Hz, 1H), 9.33 (d, J=1.10 Hz, 1H); ESIMS found for $C_{27}H_{23}FN_8O$ m/z 495.5 (M+1).

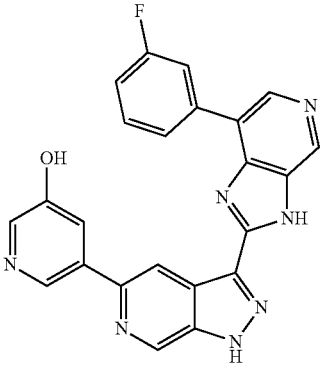
896



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine 896.

Yellow solid (49.6 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 3.96 (s, 3H), 7.30 (td, J=8.51, 2.20 Hz, 1H), 7.56-7.65 (m, 1H), 7.99-8.04 (m, 1H), 8.17 (br d, J=7.68 Hz, 1H), 8.33 (d, J=2.74 Hz, 1H), 8.42 (br d, J=10.15 Hz, 1H), 8.67 (s, 1H), 8.85 (s, 1H), 8.92 (s, 2H), 9.27 (d, J=0.82 Hz, 1H); ESIMS found for $C_{24}H_{16}FN_7O$ m/z 438.1 (M+1).

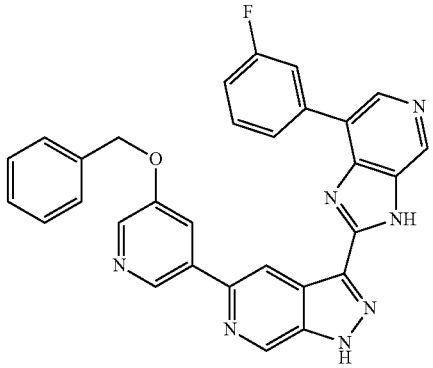
897



5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol 897.

Brown solid (18.1 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.33 (td, J=8.51, 2.47 Hz, 1H), 7.60-7.68 (m, 1H), 7.90 (t, J=2.20 Hz, 1H), 8.20 (d, J=2.74 Hz, 1H), 8.22-8.31 (m, 1H), 8.42 (br s, 1H), 8.75 (br s, 1H), 8.79 (d, J=1.65 Hz, 1H), 8.94 (br s, 2H), 9.32 (s, 1H), 10.07 (br s, 1H), 13.97 (br s, 1H), 14.30 (br s, 1H); ESIMS found for $C_{23}H_{14}FN_7O$ m/z 424.1 (M+1).

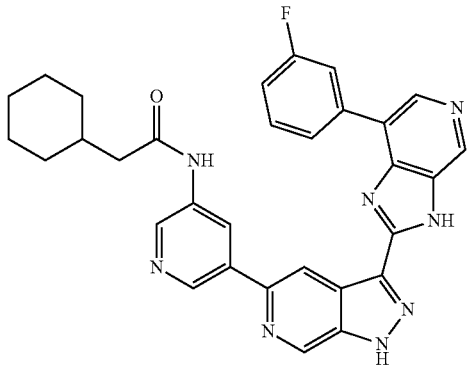
898



5-(5-(Benzyloxy)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 898.

Off-white solid (53 mg, 0.098 mmol, 61.0% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 5.31 (s, 2H), 7.17 (br s, 1H), 7.34-7.41 (m, 1H), 7.45 (t, J=7.41 Hz, 2H), 7.55 (d, J=6.86 Hz, 2H), 7.57-7.64 (m, 1H), 8.08-8.13 (m, 1H), 8.22 (br s, 1H), 8.34-8.43 (m, 1H), 8.44 (d, J=2.74 Hz, 1H), 8.74 (br s, 1H), 8.91 (br s, 1H), 8.96 (d, J=1.65 Hz, 1H), 8.99 (br s, 1H), 9.34 (d, J=1.10 Hz, 1H), 13.93 (br s, 1H), 14.45 (br s, 1H); ESIMS found for $C_{30}H_{20}FN_7O$ m/z 514.2 (M+1).

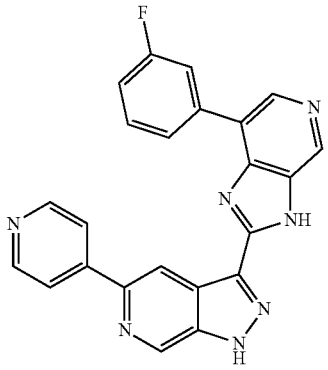
899



2-Cyclohexyl-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide 899.

Dark brown solid (10 mg, 0.016 mmol, 34.6% yield). ^{1}H NMR (DMSO-d6, 500 MHz) δ ppm 0.97-1.08 (m, 2H), 1.11-1.32 (m, 3H), 1.63 (br d, J=11.53 Hz, 1H), 1.69 (br d, J=12.62 Hz, 2H), 1.75 (br d, J=11.53 Hz, 2H), 1.83 (ddd, J=11.05, 7.48, 3.70 Hz, 1H), 2.29 (d, J=7.14 Hz, 2H), 7.30 (br t, J=8.37 Hz, 1H), 7.66 (br d, J=6.86 Hz, 1H), 8.27 (br d, J=7.68 Hz, 1H), 8.41 (br d, J=9.61 Hz, 1H), 8.78 (br s, 2H), 8.90 (br s, 2H), 8.97 (br d, J=9.60 Hz, 2H), 9.35 (s, 1H), 10.24 (s, 1H), 13.91 (br s, 1H), 14.56 (br s, 1H); ESIMS found for $C_{31}H_{27}FN_8O$ m/z 547.2 (M+1).

900

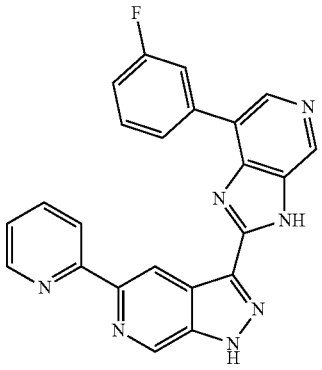


3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine 900.

Off-white solid (17.0 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.32-7.41 (m, 1H), 7.62-7.71 (m, 1H), 8.11 (d, J=6.04 Hz, 2H), 8.16 (br s, 1H), 8.54 (br s, 1H), 8.70-8.75 (m, 2H), 8.76 (br s, 1H), 8.92 (br s, 1H), 9.12 (br

s, 1H), 9.35 (d, J=0.82 Hz, 1H); ESIMS found for $C_{23}H_{14}FN_7$ m/z 408.1 (M+1).

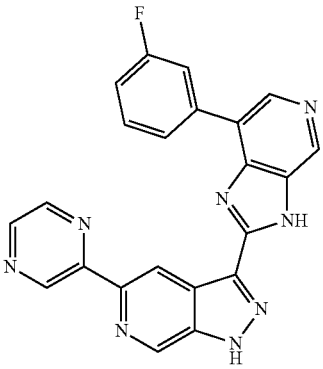
901



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine 901.

White solid (25 mg, 0.058 mmol, 65.1% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.29-7.39 (m, 1H), 7.41-7.49 (m, 1H), 7.66 (br d, J=6.59 Hz, 1H), 7.97 (td, J=7.68, 1.65 Hz, 1H), 8.26 (br s, 1H), 8.42 (br s, 1H), 8.46 (d, J=7.96 Hz, 1H), 8.75 (br d, J=3.84 Hz, 2H), 8.91 (br s, 1H), 9.29 (d, J=0.82 Hz, 1H), 9.60 (br s, 1H), 13.90 (br s, 1H), 14.50 (br s, 1H); ESIMS found for $C_{23}H_{14}FN_7$ m/z 408.1 (M+1).

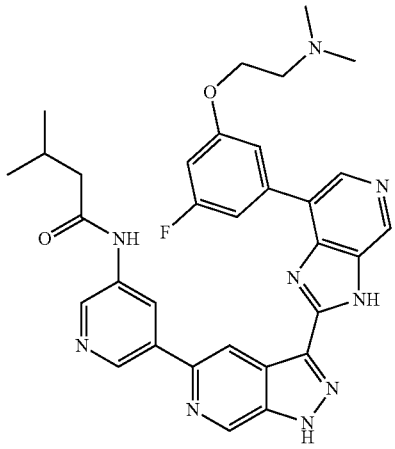
902



3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine 902.

Brown solid (23 mg, 0.054 mmol, 43.9% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.31-7.40 (m, 1H), 7.60-7.72 (m, 1H), 8.25 (br s, 1H), 8.42 (br d, J=9.61 Hz, 1H), 8.72 (d, J=2.47 Hz, 1H), 8.80 (br s, 2H), 8.91 (br s, 1H), 9.36 (s, 1H), 9.58 (br s, 1H), 9.63 (s, 1H), 13.94 (br s, 1H), 14.61 (br s, 1H); ESIMS found for $C_{22}H_{13}FN_8$ m/z 409.1 (M+1).

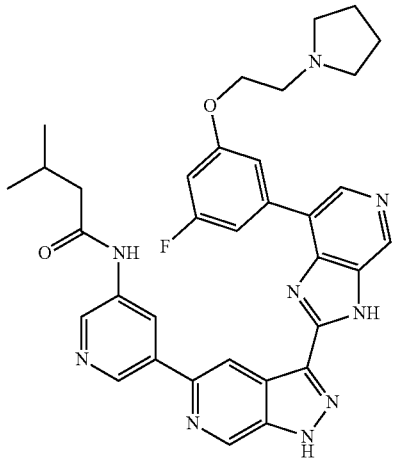
1192



N-(5-(3-(7-(3-(2-(Dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 1192.

Yellow solid (10.7 mg, 0.018 mmol, 21.81% yield). ^{1}H NMR (DMSO-d6, 500 MHz) δ ppm 0.97 (br d, J=6.59 Hz, 6H), 2.07-2.22 (m, 7H), 2.27 (br d, J=7.14 Hz, 2H), 2.61 (br s, 2H), 4.20 (br t, J=5.49 Hz, 2H), 6.93 (br d, J=10.43 Hz, 1H), 7.91 (br s, 2H), 8.76 (br s, 1H), 8.84 (s, 2H), 8.93 (br d, J=9.61 Hz, 3H), 9.35 (s, 1H), 10.24 (s, 1H), 13.98 (brs, 1H), 14.40 (brs, 1H); ESIMS found for $C_{32}H_{32}FN_9O_2$ m/z 594.3 (M+1).

1236

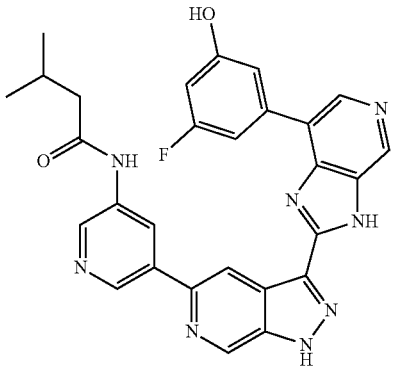


N-(5-(3-(7-(3-Fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 1236.

Yellow solid (3.7 mg, 5.97 μmol, 11.67% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.97 (d, J=6.59 Hz, 6H), 1.61 (br s, 4H), 2.12 (dquin, J=13.53, 6.77, 6.77, 6.77, 6.77 Hz, 1H), 2.27 (d, J=7.14 Hz, 2H), 2.45 (br s, 4H), 2.74 (br s, 2H), 4.20 (t, J=6.04 Hz, 2H), 6.89-6.96 (m, 1H), 7.87 (br s, 2H), 8.74 (br s, 1H), 8.83 (s, 2H), 8.91 (br s, 2H), 8.93 (br s, 1H), 9.34 (d, J=1.10 Hz, 1H), 10.23 (s, 1H), 14.11 (brs, 1H);

ESIMS found for $C_{34}H_{34}FN_9O_2$ m/z 620.3 (M+1).

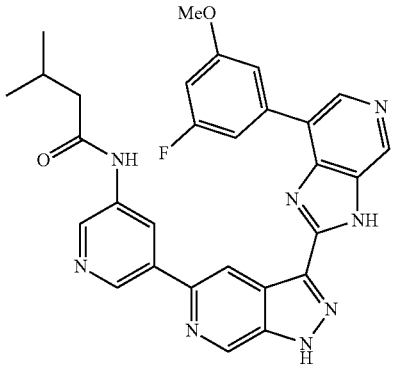
1280



N-(5-(3-(7-(3-Fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 1280.

Yellow solid (28.8 mg, 0.055 mmol, 74.3% yield). ^{1}H NMR (DMSO-d6, 500 MHz) δ ppm 0.98 (d, J=6.59 Hz, 6H), 2.13 (dquin, J=13.62, 6.75, 6.75, 6.75, 6.75 Hz, 1H), 2.28 (d, J=7.14 Hz, 2H), 6.64-6.73 (m, 1H), 7.69-7.84 (m, 2H), 8.68 (br s, 1H), 8.79-8.93 (m, 3H), 8.96-9.05 (m, 2H), 9.35 (s, 1H), 10.13 (br s, 1H), 10.20 (br s, 1H), 13.88 (br s, 1H), 14.55 (br s, 1H); ESIMS found for $C_{28}H_{23}FN_8O_2$ m/z 523.2 (M+1).

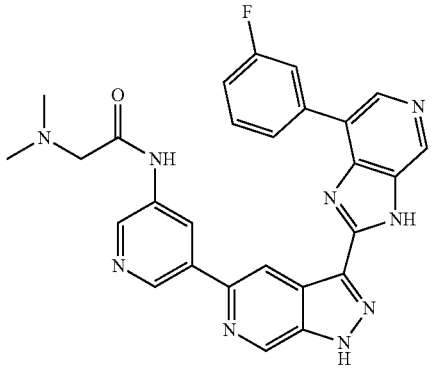
1324



N-(5-(3-(7-(3-Fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide 1324.

Yellow solid (16.8 mg, 0.031 mmol, 32.9% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.98 (d, J=6.59 Hz, 6H), 2.13 (dquin, J=13.70, 6.73, 6.73, 6.73, 6.73 Hz, 1H), 2.28 (d, J=7.14 Hz, 2H), 3.92 (s, 3H), 6.93 (dt, J=10.84, 2.26 Hz, 1H), 7.88 (br s, 1H), 8.07 (br s, 1H), 8.75-8.86 (m, 2H), 8.88 (br s, 2H), 8.95 (br s, 1H), 8.98 (d, J=1.92 Hz, 1H), 9.35 (s, 1H), 10.23 (s, 1H), 13.92 (br s, 1H), 14.57 (br s, 1H); ESIMS found for $C_{29}H_{25}FN_8O_2$ m/z 537.2 (M+1).

1367



2-(Dimethylamino)-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide 1367.

Black solid (5.9 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.53 (br s, 6H), 3.52 (br s, 2H), 7.32 (br t, J=7.55 Hz, 1H), 7.61-7.71 (m, 1H), 8.25 (br d, J=8.51 Hz, 1H), 8.44 (br d, J=8.23 Hz, 1H), 8.79 (br s, 1H), 8.86 (br s, 1H), 8.91 (br s, 2H), 8.98 (br s, 1H), 9.03 (s, 1H), 9.36 (s, 1H), 10.38 (br s, 1H), 13.90 (br s, 1H), 14.57 (br s, 1H); ESIMS found for $C_{27}H_{22}FN_9O$ m/z 508.2 (M+1).

Example 2

The screening assay for Wnt activity is described as follows. Reporter cell lines can be generated by stably transducing cancer cell lines (e.g., colon cancer) or primary cells (e.g., IEC-6 intestinal cells) with a lentiviral construct that includes a Wnt-responsive promoter driving expression of the firefly luciferase gene.

SW480 colon carcinoma cells were transduced with a lentiviral vector expressing luciferase with a human Sp5 promoter consisting of a sequence of eight TCF/LEF binding sites. SW480 cells stably expressing the Sp5-Luc reporter gene and a hygromycin resistance gene were selected by treatment with 150 μg/ml of hygromycin for 7 days. These stably transduced SW480 cells were expanded in cell culture and used for all further screening activities. For Sp5-Luc reporter gene assays, the cells were plated at 10,000 cells/well in 96-well plates with growth medium containing 10% fetal calf serum and incubated overnight at 37° C. and 5% CO_2. Each compound was dissolved in DMSO as a 10 mM stock in standard j-vials and used to prepare compound source plates in dose-response format with 3-fold serial dilutions and a 10 mM top concentration. Compound transfer from serially diluted source plates to assay plates containing the cells was accomplished using a pintool (Multimek 96, Beckman equipped with V&P Scientific FP1S50H pins) based liquid handling protocol. This protocol used a slotted pin to transfer 50 nl of compound from a source plate well to an assay plate well containing 50 μl of cells in growth medium. The 1000-fold dilution resulted in a final DMSO concentration of 0.1% on the cells in each well. Control wells received 50 nl of DMSO treatment for normalization and calculating IC_{50} values. The treated cells were incubated at 37° C. and 5% CO_2 for an additional forty-two hours. Following incubation, the growth medium was removed and 50 μl of BrightGlo luminescence reagent (Promega) was added to each well of the 96-well assay plates. The plates were placed on an orbital shaker for 5 min and then luminescence was quantified on the Victor3 (Perkin Elmer) plate reader. Readings were normalized to DMSO only treated cells, and normalized

activities were utilized for IC_{50} calculations using the dose-response log (inhibitor) vs. response–variable slope (four parameters) nonlinear regression feature available in GraphPad Prism 5.0 or 6.0. Table 2 shows the measured activity for selected compounds of Formula I as described herein.

TABLE 2

Compound	IC_{50} (μM)	Compound	IC_{50} (μM)	Compound	IC_{50} (μM)
1	0.0610	148	>10	358	0.0067
2	0.1200	154	0.9449	359	0.0335
6	0.0135	157	0.8661	395	0.0467
7	0.0718	163	0.3104	401	0.7740
8	0.0411	169	0.1218	407	0.0239
13	0.0801	175	0.8196	410	0.0296
17	0.0170	181	0.0448	413	0.0580
18	0.0294	211	>10	416	>10
19	0.0216	217	0.5574	423	0.4817
25	0.0311	223	1.3850	428	0.1753
28	0.1697	229	0.4404	434	0.2271
32	0.0143	234	0.3793	440	1.2060
34	0.1744	239	0.0400	885	>10
40	1.0650	245	0.1466	886	1.943
43	0.0767	251	0.0330	887	0.006
44	0.1645	257	0.6529	888	0.070
46	0.1654	266	>10	889	0.552
52	0.1788	272	0.0376	890	0.103
55	0.0704	278	0.1153	891	0.735
58	0.0402	284	0.2613	892	>10
60	0.0470	287	0.0306	893	>10
61	0.1230	288	0.079	894	>10
68	0.1670	293	0.3189	895	0.437
69	0.0703	299	0.5875	896	0.031
70	0.1272	305	0.0351	897	0.059
72	0.1441	311	0.0705	898	0.520
73	0.1555	314	0.0074	899	1.740
79	>10	320	0.0037	900	0.065
82	>10	326	0.7720	901	0.805
87	>10	332	0.0328	902	0.050
90	0.0935	341	0.0058	1192	>10
93	2.8470	344	0.0254	1236	>10
101	0.2941	346	0.0170	1280	>10
109	>10	347	0.0075	1324	0.547
121	>10	353	1.0390	1367	0.512
136	0.5619	355	0.0065		
141	>10	356	0.0176		

Example 3

The above synthesized compounds were screened using primary human mesenchymal stem cells (hMSCs) to determine their ability to induce chondrogenesis (process by which cartilage is developed).

Human Mesenchymal Stem Cell Culture:

Primary human mesenchymal stem cells (hMSCs) were purchased from Lonza (Walkersville, Md.) and expanded in Mesenchymal Stem Cell Growth Media (Lonza). Cells between passage 3 and 6 were used for the experiments.

Compound Screening:

Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 6-point dose-response curves from 2700 nM to 10 nM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, Calif.) into 96-well clear bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.03%. hMSCs were plated at 20,000 cells/well in 250 μL/well Incomplete Chondrogenic Induction Medium (Lonza; DMEM, dexamethasone, ascorbate, insulin-transferrin-selenium [ITS supplement], gentamycin-amphotericin [GA-1000], sodium pyruvate, proline and L-glutamine). TGF-β3 (10 ng/mL) was used as a positive control for differentiation while negative control wells were treated with 75 nL DMSO for normalization and calculating EC_{50} values. Cells were incubated at 37° C. and 5% CO_2 for 6 days. To image chondrogenic nodules, the cells were fixed using 4% formaldehyde (Electron Microscopy Sciences), and stained with 2 μg/mL Rhodamine B (Sigma-Aldrich) and 20 μM Nile Red (Sigma-Aldrich) [Johnson K., et. al, A Stem Cell-Based Approach to Cartilage Repair, *Science*, (2012), 336(6082), 717-721]. The nodules imaged (4 images per well at 4× magnification) by excitation at 531 nm and emission at 625 nm and quantified using the CellInsight CX5 (Thermo Scientific). Number of nodules in each well was normalized to the average of 3 DMSO treated wells on the same plate using Excel (Microsoft Inc.). The normalized averages (fold change over DMSO) of 3 replicate wells for each compound concentration were calculated. Due to solubility limitations of some of the compounds, curve fitting was incomplete leading to inaccurate EC_{50} determinations.

Using TGF-β3 as a positive control, the concentration of test compounds required to induce equivalent levels of chondrogenesis is reported. In addition, the maximum activity of each compound and the respective dose that each compound reached maximum chondrogenesis activity is reported. Table 3 shows the activity of selected compounds as provided herein.

TABLE 3

Compound	Conc (nM) of Max. activity	Max. Activity as % TGF-β3 activity	Conc (nM) of 100% TGF-β3 activity
6	900	300	136.2
32	2700	2700	110.4
181	30	10	100.1
251	30	N/A	42.0
287	300	300	84.2
314	900	900	180.2
320	300	N/A	41.0
341	100	100	161.9
358	100	100	230.8
407	30	30	79.2
888	100	100	71.0
896	300	300	140.4

Example 4

The above synthesized compounds were screened using primary human fibroblasts (derived from IPF patients) treated with TGF-β1 to determine their ability to inhibit the fibrotic process.

Human Fibroblast Cell Culture:

Primary human fibroblasts derived from IPF patients (LL29 cells) [[1]Xiaoqiu Liu, et. al., "Fibrotic Lung Fibroblasts Show Blunted Inhibition by cAMP Due to Deficient cAMP Response Element-Binding Protein Phosphorylation", *Journal of Pharmacology and Experimental Therapeutics* (2005), 315(2), 678-687; [2]Watts, K. L., et. al., "RhoA signaling modulates cyclin D1 expression in human lung fibroblasts; implications for idiopathic pulmonary fibrosis", *Respiratory Research* (2006), 7(1), 88] were obtained from American Type Culture Collection (ATCC) and expanded in F12 medium supplemented with 15% Fetal Bovine Serum and Penicillin/Streptomycin.

Compound Screening:

Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:2, 11-point dose-response curves from 10 μM to

1.87 nM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, Calif.) into 384-well clear bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.1%. LL29 cells were plated at 1,500 cells/well in 80 l/well F12 medium supplemented with 1% Fetal Bovine Serum. One hour after addition of the cells, TGF-β1 (Peprotech; 20 ng/mL) was added to the plates to induce fibrosis (ref. 1 and 2 above). Wells treated with TGF-β1 and containing DMSO were used as controls. Cells were incubated at 37° C. and 5% CO_2 for 4 days. Following incubation for 4 days, SYTOX green nucleic acid stain (Life Technologies [Thermo Fisher Scientific]) was added to the wells at a final concentration of 1 uM and incubated at room temperature for 30 min. Cells were then fixed using 4% formaldehyde (Electron Microscopy Sciences), washed 3 times with PBS followed by blocking and permeabilization using 3% Bovine Serum Albumin (BSA; Sigma) and 0.3% Triton X-100 (Sigma) in PBS. Cells were then stained with antibody specific to α-smooth muscle actin (αSMA; Abcam) (ref. 1 and 2 above) in 3% Bovine Serum Albumin (BSA; Sigma) and 0.3% Triton X-100 (Sigma) in PBS, and incubated overnight at 4° C. Cells were then washed 3 times with PBS, followed by incubation with Alexa Flor-647 conjugated secondary antibody (Life Technologies [Thermo Fisher Scientific]) and DAPI at room temperature for 1 hour. Cells were then washed 3 times with PBS and plates were sealed for imaging. αSMA staining was imaged by excitation at 630 nm and emission at 665 nm and quantified using the Compartmental Analysis program on the CellInsight CX5 (Thermo Scientific). Dead or apoptotic cells were excluded from analysis based on positive SYTOX green staining. % of total cells positive for αSMA were counted in each well and normalized to the average of 11 wells treated with TGF-β1 on the same plate using Dotmatics' Studies Software. The normalized averages (fold change over untreated) of 3 replicate wells for each compound concentration were used to create dose-responses curves and EC_{50} values were calculated using non-linear regression curve fit in the Dotmatics' Studies Software. The EC_{50} values are reported.

Table 4 shows the activity of selected compounds as provided herein.

TABLE 4

Compound	Inhibition of fibrosis EC_{50} (nM)	Compound	Inhibition of fibrosis EC_{50} (nM)	Compound	Inhibition of fibrosis EC_{50} (nM)
6	0.511	169	0.074	355	0.148
7	0.009	175	0.009	356	0.110
8	0.047	181	0.009	358	0.019
13	0.009	211	0.009	359	0.689
18	0.143	217	9.990	395	0.009
25	0.009	223	9.990	401	9.990
32	0.009	229	9.990	407	>10
40	1.767	234	0.966	410	0.475
43	0.076	239	0.009	413	9.990
44	0.075	245	9.990	416	9.990
52	1.197	251	0.009	423	2.033
55	0.009	257	2.626	428	9.990
58	0.041	266	9.990	434	8.265
60	9.990	272	0.009	440	0.009
69	0.044	284	0.908	885	9.990
72	0.009	287	0.319	886	0.072
73	4.332	293	0.009	888	0.009
79	0.018	299	0.009	889	0.046
82	9.990	305	>10	890	0.088
93	9.990	311	0.254	893	9.990
101	9.990	314	0.173	895	9.990
109	9.990	320	0.103	896	0.009
121	9.990	326	0.009	897	0.032
136	0.598	332	1.050	900	0.009
141	9.990	341	0.009	901	0.584
148	9.990	344	0.060	1280	0.009
154	0.649	346	0.030	1324	0.009
157	1.562	347	0.009	1367	0.144
163	0.038	353	0.251		

Example 5

The above synthesized compounds were screened using ARPE-19 cells [a spontaneously arising retinal pigment epithelia (RPE) cell line] to determine their ability to trans-differentiate ARPE-19 into eye neuronal cells [photoreceptors].

ARPE-19 Cell Culture:

ARPE-19 cells are cultured in standard culture medium containing Dulbecco's Modified Eagle's Medium and Ham's F12 Nutrient Mixture (DMEM/F12) mix (1:1)+ GlutaMax with 1% penicillin-Streptomycin and 10% FBS (Fetal Bovine Serum). Cells are incubated at 37° C. with 5% CO_2. Cells are trypsinized and plated onto 384-well pre-spotted plate at a density of 3000 cells/well in 50 uL of media. Plating media: DMEM/F12 (1:1)+3% charcoal filtered-FBS+GlutaMax+1% pen/Strep. Cells are incubated at 37° C. with 5% CO_2. At 40 hours, cells were fixed for 15 min with 10% Buffered Formalin. Cells were then washed 3 times with PBS for 5 min each, permeablize using 0.3% Triton X-100 in 1×PBS for 30 min, block for 1 hr with 2% BSA in 1×PBS with 0.1% Triton X-100. The primary antibody (1:100 PAX6 Santa Cruz Biotech; sc-81649) was diluted and 10 μL/well was added to the cells. The cells were incubated overnight at 4° C. The plates were washed 3× with PBS before applying the secondary antibody (goat Anti-mouse 488), shake for 1 hr in complete darkness, aspirate secondary, add 10 μL of DAPI (diamidino-2-phenylindole) (1 μg/mL), shake for 10 min. Wash 3× in PBS and scan on Thermo Fisher Scientific cell-Insight CX5. Readings were normalized to DMSO only treated cells, and normalized activities were utilized for EC_{50} calculations using the dose-response log (activator) vs. response–variable slope (four parameters) nonlinear regression feature available in GraphPad Prism 5.0 or 6.0.

Table 5 shows the activity of selected compounds as provided herein.

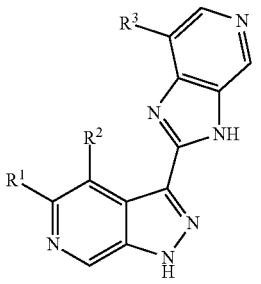
TABLE 5

Compound	EC_{50} (μM)
890	0.009
895	0.1616

What is claimed is:

1. A compound, or a pharmaceutically acceptable salt thereof, of Formula I:

I



wherein:

R^1 is selected from the group consisting of -heteroaryl $(R^4)_q$ and -heterocyclyl$(R^5)_h$;

R^2 is selected from the group consisting of H and halide;

R^3 is selected from the group consisting of -heteroaryl $(R^6)_q$, -heterocyclyl$(R^7)_h$, and -aryl$(R^8)_k$;

each R^4 is one substituent attached to the heteroaryl and is independently selected from the group consisting of halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl $(R^9)_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{10})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{11})_k$, —NHC(=O)R^{12}, —$R^{13}R^{14}$, $(C_{1-6}$ alkylene)$NR^{15}R^{16}$, and —OR^{22};

each R^5 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —OCH_3, —CN, and —C(=O)R^{17};

each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, and —OCH_3;

each R^8 is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, —OCH_3, —$(C_{1-6}$ alkylene$)_p$$NHSO_2R^{17}$, —$NR^{13}(C_{1-6}$ alkylene) $NR^{13}R^{14}$; —$(C_{1-6}$ alkylene$)_p$$NR^{13}R^{14}$, and —$OR^{25}$;

each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{10} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{11} is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{12} is independently selected from the group consisting of —$(C_{1-9}$ alkyl), -heteroaryl$(R^{18})_q$, -aryl$(R^{19})_k$, —CH_2aryl$(R^{19})_k$, -carbocyclyl$(R^{20})_j$, —CH_2carbocyclyl$(R^{20})_j$, —$(C_{1-4}$ alkylene$)_p$$NR^{23}R^{24}$, -heterocyclyl$(R^{21})_h$, and —$CH_2$heterocyclyl$(R^{21})_h$;

each R^{13} is independently selected from the group consisting of H and —$(C_{1-6}$ alkyl);

each R^{14} is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), —CH_2aryl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$;

each R^{15} is independently selected from the group consisting of H and —$(C_{1-6}$ alkyl);

each R^{16} is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), —CH_2aryl$(R^{19})_k$, and —CH_2carbocyclyl$(R^{20})_j$;

each R^{17} is a —$(C_{1-6}$ alkyl);

each R^{18} is one substituent attached to the heteroaryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{19} is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{20} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

each R^{21} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN;

R^{22} is selected from the group consisting of H, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{21})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{20})_j$, —$(C_{1-4}$ alkylene$)_p$aryl $(R^{19})_k$, and —$(C_{1-6}$ alkylene$)_p$$NR^{23}R^{24}$;

each R^{23} is independently selected from the group consisting of H and —$(C_{1-6}$ alkyl);

each R^{24} is independently selected from the group consisting of H and —$(C_{1-6}$ alkyl);

R^{25} is selected from the group consisting of H, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{21})_h$, and —$(C_{1-6}$ alkylene$)_p$$NR^{23}R^{24}$;

each p is independently 0 or 1;

each q is independently 0 to 4;

each h is independently 0 to 10;

each k is independently 0 to 5; and

each j is independently 0 to 12.

2. A pharmaceutical composition comprising a compound according to claim **1**, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

3. The compound of claim **1**, wherein R^1 is -heteroaryl $(R^4)_q$.

4. The compound of claim **3**, wherein R^1 is selected from the group consisting of -pyridinyl$(R^4)_q$, -pyrimidinyl$(R^4)_q$, -pyrazolyl$(R^4)_q$, and -imidazolyl$(R^4)_q$.

5. The compound of claim **3**, wherein q is 0, 1 or 2.

6. The compound of claim **5**, wherein R^4 is selected from the group consisting of —$(C_{1-3}$ alkyl), —CH_2heterocyclyl $(R^9)_h$, —NHC(=O)R^{12}, —$NR^{13}R^{14}$, —$CH_2NR^{15}R^{16}$, and —OR^{22}.

7. The compound of claim **1**, wherein R^3 is -aryl$(R^8)_k$.

8. The compound of claim **7**, wherein R^3 is -phenyl$(R^8)_k$.

9. The compound of claim **7**, wherein k is 1, or 2.

10. The compound of claim **9**, wherein each R^8 is independently selected from the group consisting of halide and is —$CH_2NHSO_2R^{17}$.

11. The compound of claim **1**, wherein R^3 is -heteroaryl $(R^6)_q$.

12. The compound of claim **11**, wherein R^3 is selected from the group consisting of -pyridinyl$(R^6)_q$, -imidazolyl $(R^6)_q$, -furanyl$(R^6)_q$, and -thiophenyl$(R^6)_q$.

13. The compound of claim **11**, wherein q is 0 or 1.

14. The compound of claim **13**, wherein q is 1 and R^6 is selected from the group consisting of halide, —$(C_{1-3}$ alkyl), and —C(=O)R^{17}.

15. The compound of claim **1**, wherein R^3 is -heterocyclyl $(R^7)_h$.

16. The compound of claim **15**, wherein R^3 is selected from the group consisting of -piperidinyl$(R^7)_h$, -morpholinyl $(R^7)_h$, and -piperazinyl$(R^7)_h$.

17. The compound of claim 16, wherein h is 0, 1, or 2.

18. The compound of claim 17, wherein each R^7 is independently selected from the group consisting of a halide and —(C_{1-3} alkyl).

19. The compound of claim 1, wherein R^2 is H.

20. The compound of claim 1, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) propionamide [1];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [2];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [3];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [4];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [5];

N-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) methyl)ethanamine [6];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethyl-pyridin-3-amine [7];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) pivalamide [8];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) isobutyramide [9];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [10];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) benzamide [11];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [12];

1-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [13];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo [3,4-c]pyridine [14];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [15];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [16];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [17];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) pentanamide [18];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [19];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [20];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [21];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [22];

N-benzyl-1-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [23];

1-cyclopentyl-N-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl) pyridin-3-yl)methyl)methanamine [24];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [25];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [26];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) propionamide [27];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [28];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [29];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [30];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [31];

N-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) methyl)ethanamine [32];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethyl-pyridin-3-amine [33];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) pivalamide [34];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) isobutyramide [35];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [36];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) benzamide [37];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [38];

1-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [39];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo [3,4-c]pyridine [40];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [41];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [42];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [43];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) pentanamide [44];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [45];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [46];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [47];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [48];

N-benzyl-1-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [49];

1-cyclopentyl-N-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl) pyridin-3-yl)methyl)methanamine [50];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [51];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [52];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) propionamide [53];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [54];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [55];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [56];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [57];

N-((5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) methyl)ethanamine [58];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethyl-pyridin-3-amine [59];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) pivalamide [60];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) isobutyramide [61];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [62];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) benzamide [63];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [64];

1-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [65];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo [3,4-c]pyridine [66];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [67];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [68];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [69];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) pentanamide [70];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [71];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [72];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [73];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [74];

N-benzyl-1-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [75];

1-cyclopentyl-N-((5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl) pyridin-3-yl)methyl)methanamine [76];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [77];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [78];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [79];

3-methyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [80];

5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [81];

5-(pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [82];

5-(4-methylpyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [83];

N-((5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) methyl)ethanamine [84];

N,N-dimethyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [85];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [86];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl) isobutyramide [87];

2-phenyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [88];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [89];

N-isopropyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [90];

N,N-dimethyl-1-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [91];

3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [92];

5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [93];

3,3-dimethyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [94];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [95];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [96];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [97];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [98];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [99]; and

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [100]; or a pharmaceutically acceptable salt thereof.

21. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-benzyl-1-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [101];

1-cyclopentyl-N-((5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [102];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [103];

3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [104];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [105];

3-methyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [106];

5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [107];

5-(pyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [108];

5-(4-methylpyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [109];

N-((5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [110];

N,N-dimethyl-5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [111];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [112];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [113];

2-phenyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [114];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [115];

N-isopropyl-5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [116];

N,N-dimethyl-1-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [117];

3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [118];

5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [119];

3,3-dimethyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [120];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [121];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [122];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [123];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [124];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [125];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [126];

N-benzyl-1-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [127];

1-cyclopentyl-N-((5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [128];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [129];

3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [130];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [131];

3-methyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [132];

5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [133];

3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [134];

5-(4-methylpyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [135];

N-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [136];

N,N-dimethyl-5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [137];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [138];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [139];

2-phenyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [140];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [141];

N-isopropyl-5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [142];

N,N-dimethyl-1-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [143];

3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [144];

5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [145];

3,3-dimethyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [146];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [147];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [148];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [149];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [150];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [151];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [152];

N-benzyl-1-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [153];

1-cyclopentyl-N-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [154];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [155];

3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [156];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [157];

3-methyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [158];

5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [159];

3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [160];

5-(4-methylpyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [161];

N-((5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [162];

N,N-dimethyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [163];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [164];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [165];

2-phenyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [166];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [167];

N-isopropyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [168];

N,N-dimethyl-1-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [169];

3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [170];

3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [171];

3,3-dimethyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [172];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [173];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [174];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [175];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [176];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [177];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [178];

N-benzyl-1-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [179];

1-cyclopentyl-N-((5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [180];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [181];

3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [182];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [183];

3-methyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [184];

5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [185];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [186];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [187];

N-((5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [188];

N,N-dimethyl-5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [189];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [190];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [191];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [192];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [193];

N-isopropyl-5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [194];

N,N-dimethyl-1-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [195];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [196];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [197];

3,3-dimethyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [198];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [199]; and

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [200]; or a pharmaceutically acceptable salt thereof.

22. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [201];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [202];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [203];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-A-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [204];

N-benzyl-1-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [205];

1-cyclopentyl-N-((5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-A-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [206];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-A-3-(7-(4-methyl-1H-imidazol-1-A-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [207];

3-(7-(4-methyl-1H-imidazol-1-A-3H-imidazo[4,5-c]pyridin-2-A-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [208];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [209];

3-methyl-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [210];

5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [211];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-A-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [212];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-A-1H-pyrazolo[3,4-c]pyridine [213];

N-((5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-A-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [214];

N,N-dimethyl-5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [215];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [216];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [217];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [218];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [219];

N-isopropyl-5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [220];

N,N-dimethyl-1-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [221];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [222];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [223];

3,3-dimethyl-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [224];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [225];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [226];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [227];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [228];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [229];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [230];

N-benzyl-1-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [231];

1-cyclopentyl-N-((5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [232];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [233];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [234];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [235];

3-methyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [236];

5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [237];

5-(pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [238];

5-(4-methylpyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [239];

N-((5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [240];

N,N-dimethyl-5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [241];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [242];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [243];

2-phenyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [244];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [245];

N-isopropyl-5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [246];

N,N-dimethyl-1-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [247];

5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [248];

5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [249];

3,3-dimethyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [250];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [251];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [252];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [253];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [254];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [255];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [256];

N-benzyl-1-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [257];

1-cyclopentyl-N-((5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [258];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [259];

5-(pyrimidin-5-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [260];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [261];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [262];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [263];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [264];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [265];

N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [266];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [267];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [268];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [269];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [270];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [271];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [272];

1-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [273];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [274];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [275];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [276];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [277];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [278];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [279];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3yl)cyclobutanecarboxamide [280];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [281];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [282];

N-benzyl-1-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [283];

1-cyclopentyl-N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [284];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [285];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [286];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [287];

3-methyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [288];

5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [289];

5-(pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [290];

5-(4-methylpyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [291];

N-((5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [292];

N,N-dimethyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [293];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [294];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [295];

2-phenyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [296];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [297];

N-isopropyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [298];

N,N-dimethyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [299]; and

5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [300]; or a pharmaceutically acceptable salt thereof.

23. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [301];

3,3-dimethyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [302];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [303];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [304];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [305];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [306];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [307];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [308];

N-benzyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [309];

1-cyclopentyl-N-((5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [310];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [311];

5-(pyrimidin-5-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [312];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [313];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [314];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [315];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [316];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [317];

N-((5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [318];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [319];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [320];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [321];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [322];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [323];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [324];

1-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [325];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [326];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [327];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [328];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [329];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [330];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [331];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [332];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [333];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [334];

N-benzyl-1-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [335];

1-cyclopentyl-N-((5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [336];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [337];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [338];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [339];

3-methyl-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [340];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [341];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [342];

5-(4-methylpyridin-3-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [343];

N-((5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [344];

N,N-dimethyl-5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [345];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [346];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [347];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [348];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [349];

N-isopropyl-5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [350];

N,N-dimethyl-1-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [351];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [352];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [353];

3,3-dimethyl-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butanamide [354];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [355];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [356];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [357];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [358];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [359];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [360];

N-benzyl-1-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [361];

1-cyclopentyl-N-((5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [362];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [363];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [364];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [365];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [366];

1-(5-(2-(5-(5-aminopyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [367];

1-(5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [368];

1-(5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [369];

1-(5-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [370];

1-(5-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [371];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [372];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [373];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [374];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [375];

1-(5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [376];

1-(5-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [377];

1-(5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [378];

1-(5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [379];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [380];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [381];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [382];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [383];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [384];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [385];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [386];

1-(5-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [387];

1-(5-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [388];

1-(5-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [389];

1-(5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethanone [390];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [391];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [392];

N-(3-(2-(5-(5-aminopyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [393];

N-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [394];

N-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [395];

N-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [396];

N-(3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [397];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [398];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [399]; and

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [400];
or a pharmaceutically acceptable salt thereof.

24. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [401];
N-(3-fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [402];
N-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [403];
N-(3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [404];
N-(3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [405];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [406];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [407];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [408];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [409];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [410];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [411];
N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [412];
N-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [413];
N-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [414];
N-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [415];
N-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [416];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [417];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [418];
N^1-(3-(2-(5-(5-aminopyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [419];
N^1-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [420];
N^1-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [421];
N^1-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [422];
N^1-(3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [423];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [424];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [425];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [426];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [427];
N^1-(3-fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [428];
N^1-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [429];
N^1-(3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [430];
N^1-(3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [431];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [432];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [433];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [434];
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [435];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [436];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [437];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [438];

N^1-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [439];

N^1-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [440];

N^1-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [441];

N^1-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [442];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [885];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [886];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [887];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [888];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [889];

1-(6-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [890];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [891];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [892];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [893];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [894];

2-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [895];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [896];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [897];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [898];

2-cyclohexyl-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [899]; and

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [900]; or a pharmaceutically acceptable salt thereof.

25. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [901];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [902];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [903];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [904];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [905];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [906];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [907];

1-(6-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [908];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [909];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [910];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [911];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [912];

2-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [913];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [914];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [915];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [916];

2-cyclohexyl-N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [917];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [918];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [919];

3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [920];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [921];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [922];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [923];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [924];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [925];

1-(6-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [926];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [927];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [928];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [929];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [930];

2-((5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [931];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [932];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [933];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [934];

2-cyclohexyl-N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [935];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [936];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [937];

3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [938];

5-(piperidin-4-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [939];

3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [940];

5-(1H-pyrazol-4-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [941];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [942];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [943];

1-(6-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [944];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [945];

5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [946];

2-(piperidin-4-yl)-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [947];

3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [948];

N,N-dimethyl-2-((5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [949];

5-(5-methoxypyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [950];

5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [951];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [952];

2-cyclohexyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [953];

3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [954];

5-(pyridin-2-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [955];

5-(pyrazin-2-yl)-3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [956];

5-(piperidin-4-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [957];

3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [958];

5-(1H-pyrazol-4-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [959];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [960];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [961];

1-(6-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [962];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [963];

5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [964];

2-(piperidin-4-yl)-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [965];

3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [966];

N,N-dimethyl-2-((5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [967];

5-(5-methoxypyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [968];

5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [969];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [970];

2-cyclohexyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [971];

5-(pyridin-4-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [972];

5-(pyridin-2-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [973];
5-(pyrazin-2-yl)-3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [974];
5-(piperidin-4-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [975];
3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [976];
5-(1H-pyrazol-4-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [977];
5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [978];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [979];
1-(6-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [980];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [981];
5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [982];
2-(piperidin-4-yl)-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [983];
3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [984];
N,N-dimethyl-2-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [985];
5-(5-methoxypyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [986];
5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [987];
5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [988];
2-cyclohexyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [989];
3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [990];
5-(pyridin-2-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [991];
5-(pyrazin-2-yl)-3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [992];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [993];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [994];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [995];
5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [996];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [997];
1-(6-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [998];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [999]; and
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1000]; or a pharmaceutically acceptable salt thereof.

26. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1001];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1002];
N,N-dimethyl-2-((5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1003];
5-(5-methoxypyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1004];
5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1005];
5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1006];
2-cyclohexyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1007];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1008];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1009];
3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1010];
3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1011];
3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1012];
3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1013];
3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1014];
5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1015];
1-(6-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1016];
5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1017];
3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1018];
N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1019];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1020];

N,N-dimethyl-2-((5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1021];

5-(5-methoxypyridin-3-yl)-3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1022];

5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1023];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1024];

2-cyclohexyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1025];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1026];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1027];

3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1028];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1029];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1030];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1031];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1032];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1033];

1-(6-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1034];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1035];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1036];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1037];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1038];

N,N-dimethyl-2-((5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1039];

5-(5-methoxypyridin-3-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1040];

5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1041];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1042];

2-cyclohexyl-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1043];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1044];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1045];

3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1046];

5-(piperidin-4-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1047];

5-(1,2,3,6-tetrahydropyridin-4-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1048];

5-(1H-pyrazol-4-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1049];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1050];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1051];

1-(6-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1052];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1053];

5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1054];

2-(piperidin-4-yl)-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1055];

5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1056];

N,N-dimethyl-2-((5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1057];

5-(5-methoxypyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1058];

5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1059];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1060];

2-cyclohexyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1061];

5-(pyridin-4-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1062];

5-(pyridin-2-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1063];

5-(pyrazin-2-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1064];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1065];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1066];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1067];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1068];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1069];

1-(6-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1070];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1071];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1072];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1073];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1074];

2-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1075];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1076];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1077];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1078];

2-cyclohexyl-N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1079];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1080];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1081];

3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1082];

5-(piperidin-4-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1083];

5-(1,2,3,6-tetrahydropyridin-4-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1084];

5-(1H-pyrazol-4-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1085];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1086];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1087];

1-(6-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1088];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1089];

5-(5-(piperidin-4-yloxy)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1090];

2-(piperidin-4-yl)-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1091];

5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1092];

N,N-dimethyl-2-((5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1093];

5-(5-methoxypyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1094];

5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1095];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1096];

2-cyclohexyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1097];

5-(pyridin-4-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1098];

5-(pyridin-2-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1099]; and

5-(pyrazin-2-yl)-3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1100]; or a pharmaceutically acceptable salt thereof.

27. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1101];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1102];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1103];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1104];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1105];

1-(6-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1106];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1107];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1108];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1109];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1110];

2-((5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1111];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1112];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1113];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1114];

2-cyclohexyl-N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1115];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1116];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1117];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1118];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1119];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1120];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1121];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1122];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1123];

1-(6-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1124];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1125];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1126];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1127];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1128];

N,N-dimethyl-2-((5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1129];

5-(5-methoxypyridin-3-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1130];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1131];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1132];

2-cyclohexyl-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1133];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1134];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1135];

3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1136];

1-(5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1137];

1-(5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1138];

1-(5-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1139];

1-(5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1140];

1-(5-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1141];

1-(5-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1142];

1-(5-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1143];

1-(5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1144];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1145];

1-(5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1146];

1-(5-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1147];

1-(5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1148];

1-(5-(2-(5-(5-hydroxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1149];

1-(5-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1150];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-cyclohexylacetamide [1151];

1-(5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1152];

1-(5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1153];

1-(5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)thiophen-2-yl)ethan-1-one [1154];

N-(3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1155];

N-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1156];

N-(3-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1157];

N-(3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1158];

N-(3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1159];

N-(3-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1160];

N-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1161];

N-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1162];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1163];

N-(3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1164];

N-(3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1165];

N-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1166];

N-(3-fluoro-5-(2-(5-(5-hydroxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1167];

N-(3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1168];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1169];

N-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1170];

N-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1171];

N-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [1172];

N^1-(3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1173];

N^1-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1174];

N^1-(3-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [1175];

N^1-(3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1176];

N^1-(3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [1177];

N^1-(3-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N2-dimethylethane-1,2-diamine [1178];

N^1-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [1179];

N^1-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1180];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1181];

N^1-(3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1182];

N^1-(3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [1183];

N^1-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1184];

5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1185];

N^1-(3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [1186];

2-cyclohexyl-N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1187];

N^1-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1188];

N^1-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1189];

N^1-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [1190];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [1191];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [1192];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [1193];

2-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1194];

2-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1195];

2-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1196];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [1197];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [1198];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [1199]; and

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [1200]; or a pharmaceutically acceptable salt thereof.

28. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [1201];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [1202];

2-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1203];

2-(3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1204];

2-(3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1205];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [1206];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [1207];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [1208];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [1209];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [1210];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [1211];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [1212];

2-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1213];

2-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1214];

2-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1215];

2-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1216];

2-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1217];

2-(3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1218];

2-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1219];

2-(3-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1220];

2-(3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1221];

2-(3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1222];

1-(6-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1223];

2-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1224];

2-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1225];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1226];

2-(3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1227];

2-((5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1228];

2-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1229];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1230];

2-(3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [1231];

2-cyclohexyl-N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1232];

2-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1233];

2-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [1234];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [1235];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [1236];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [1237];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1238];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1239];

N-((5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [1240];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [1241];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [1242];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [1243];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [1244];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [1245];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [1246];

1-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [1247];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1248];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1249];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [1250];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [1251];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [1252];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [1253];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [1254];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [1255];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [1256];

N-benzyl-1-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [1257];

1-cyclopentyl-N-((5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [1258];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1259];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [1260];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1261];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1262];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1263];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1264];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1265];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1266];

1-(6-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1267];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1268];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1269];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1270];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1271];

2-((5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1272];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1273];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1274];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1275];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1276];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1277];

3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1278];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [1279];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [1280];

3-(2-(5-(5-aminopyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1281];

3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1282];

3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1283];

3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1284];

3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1285];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [1286];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [1287];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [1288];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [1289];

3-fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1290];

3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1291];

3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1292];

3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1293];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [1294];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [1295];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [1296];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [1297];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [1298];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [1299]; and

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [1300]; or a pharmaceutically acceptable salt thereof.

29. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1301];

3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1302];

3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1303];

3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1304];

3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1305];

3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1306];

3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1307];

3-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1308];

3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1309];

3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1310];

3-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1311];

3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1312];

3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1313];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1314];

3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1315];

3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1316];

3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1317];

5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1318];

3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenol [1319];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1320];

3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1321];

3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)phenol [1322];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)propionamide [1323];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [1324];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [1325];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1326];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1327];

N-((5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [1328];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [1329];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [1330];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [1331];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-phenylacetamide [1332];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)benzamide [1333];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [1334];

1-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [1335];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1336];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1337];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [1338];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [1339];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pentanamide [1340];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [1341];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [1342];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopentanecarboxamide [1343];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclohexanecarboxamide [1344];

N-benzyl-1-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [1345];

1-cyclopentyl-N-((5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)methanamine [1346];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1347];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrimidin-5-yl)-1H-pyrazolo[3,4-c]pyridine [1348];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1349];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(piperidin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1350];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1351];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1352];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1353];

5-(1,2-dimethyl-1H-imidazol-5-yl)-3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1354];

1-(6-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyrazin-2-yl)azetidin-3-amine [1355];

5-(5-(cyclohexyloxy)pyridin-3-yl)-3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1356];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1357];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1358];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1359];

2-((5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1360];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1361];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-ol [1362];

5-(5-(benzyloxy)pyridin-3-yl)-3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1363];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1364];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [1365];

3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyrazin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1366];

2-(dimethylamino)-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1367];

2-(dimethylamino)-N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1368];

2-(dimethylamino)-N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1369];

2-(dimethylamino)-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1370];

2-(dimethylamino)-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1371];

2-(dimethylamino)-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1372];

2-(dimethylamino)-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1373];

2-(dimethylamino)-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1374];

2-(dimethylamino)-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1375];

2-(dimethylamino)-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1376];

2-(dimethylamino)-N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1377];

2-(dimethylamino)-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1378];

2-(dimethylamino)-N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1379];

2-(dimethylamino)-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1380];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-2-(dimethylamino)acetamide [1381];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1382];

2-(dimethylamino)-N-(5-(3-(7-(3-((2-(dimethylamino)ethypamino)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1383];

2-(dimethylamino)-N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1384];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1385];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1386];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)acetamide [1387];

4-(2-(5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)morpholine [1388];

3-(7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1389];

3-(7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1390];

4-(2-(5-(5-fluoropyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)morpholine [1391];

5-(5-fluoropyridin-3-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1392];

3-(7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-fluoropyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [1393];

5-(5-fluoropyridin-3-yl)-3-(7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1394];

5-(5-fluoropyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1395];

4-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)morpholine [1396];

3-(7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1397];

5-(1-methyl-1H-pyrazol-4-yl)-3-(7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1398];

4-(2-(5-(1-cyclopropyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)morpholine [1399];

5-(1-cyclopropyl-1H-pyrazol-4-yl)-3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1400];

5-(1-cyclopropyl-1H-pyrazol-4-yl)-3-(7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1401];

5-(1-cyclopropyl-1H-pyrazol-4-yl)-3-(7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1402];

5-(1-cyclopropyl-1H-pyrazol-4-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [1403];

4-(2-(5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)morpholine [1404];

3-(7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1405]; and

3-(7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [1406]; or a pharmaceutically acceptable salt thereof.

30. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [6];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N,N-dimethylpyridin-3-amine [7];

1-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [13];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [17];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [19];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [25];

N-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methyl)ethanamine [32];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [55];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [72];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclopropanecarboxamide [175];

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [181];

5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [211];

5-(4-methylpyridin-3-yl)-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [239];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [251];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)-N-isopropylpyridin-3-amine [272];

N,N-dimethyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [293];

N,N-dimethyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)methanamine [299];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [314];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [320];

3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [326];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [341];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [346];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [347];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [355];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [358];

N-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)benzyl)methanesulfonamide [395];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [407];

N^1-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-pyrazolo[3,4-c]pyridin-3-yl)-3H-imidazo[4,5-c]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [440];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [887];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [888];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(5-methoxypyridin-3-yl)-1H-pyrazolo[3,4-c]pyridine [896];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(pyridin-4-yl)-1H-pyrazolo[3,4-c]pyridine [900];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [1280]; and

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [1324]; or a pharmaceutically acceptable salt thereof.

31. The compound of claim **1**, wherein the compound of Formula I is selected from the group consisting of:

5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-3-(7-(piperidin-1-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridine [181];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [251];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)-3-methylbutanamide [314];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)pivalamide [320];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-amine [341];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)isobutyramide [347];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [355];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)cyclobutanecarboxamide [358];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-1H-pyrazolo[3,4-c]pyridin-5-yl)pyridin-3-yl)butyramide [407];

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [887]; and

3-(7-(3-fluorophenyl)-3H-imidazo[4,5-c]pyridin-2-yl)-5-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo[3,4-c]pyridine [888]; or a pharmaceutically acceptable salt thereof.

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